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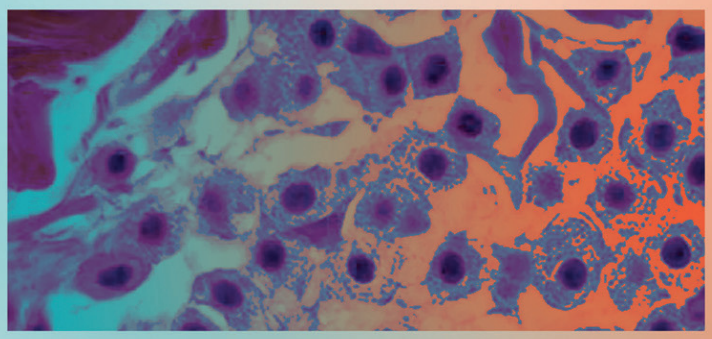
LEUKEMIA RESEARCH

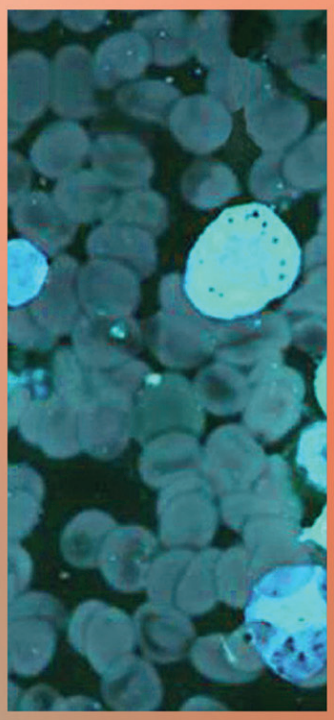
CLINICAL AND LABORATORY STUDIES

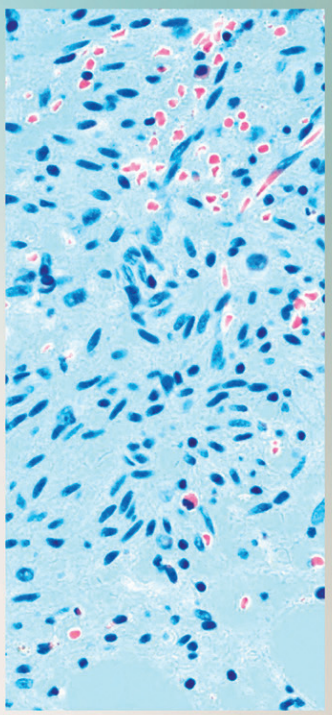
Supplement

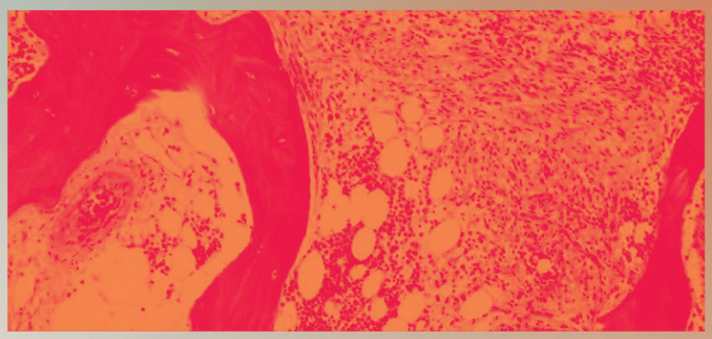
Abstracts of the
Xth Eurasian Hematology
Oncology Congress

8–11 October 2019
Istanbul, Turkey









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Leukemia Research

Clinical and Laboratory Studies

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Aims and Scope

leukemia Research is an international journal which brings comprehensive and current information to all health care professionals involved in basic and (or) applied clinical research in leukemias, lymphomas, multiple myeloma and other hematologic malignancies. The editors encourage the submission of articles relevant to normal and leukemic hemopoiesis, biochemistry, cell biology, immunology and molecular biology as well as epidemiologic and clinical studies.

Specifically, of major interest will be articles that encompass the application of oncogenes, growth factors, cell markers, cell cycle and differentiation agents, novel therapeutics and clinical trials in both the acute and chronic leukemias as well as the myelodysplastic syndromes. In addition, we solicit selected articles on the rapidly increasing specialty of marrow or stem cell reconstitution after high dose therapy with curative attempt in patients with a wide range of neoplasms.

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Clinical and Laboratory Studies

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Welcome Address

Distinguished Colleagues,

The Hematology Specialist Association has been expanding its network to the Americas and EMEA with a brand-new concept named EHOG (Eurasian Hematology-Oncology Group).

Eurasian Hematology-Oncology Group is a non-profit organization established to build a bridge in the field of hematology and oncology between these regions.

The main core of this formation is the HSA (Hematology Specialist Association), but the goal is to transform EHOG into an international society in the future.

We believe that EHOG will fill a gap in these regions not only in a scientific way but also culturally. Our main objective is to bring together scientists from different countries, to know each other and to start joint projects and studies in the future.

Hematologists and Oncologists within these countries will gather for the Xth Eurasian Hematology Oncology Congress in a unique city like Istanbul where the two continents meet. EHOC 2019 takes place in the heart of this metropolitan at the Hilton Istanbul Bosphorus between 8–11 October 2019.

A great number of abstracts and case reports were submitted to the congress which has been evaluated by a distinguished international reviewing committee. There will be nine Meet the Professor sessions, nine oral presentation sessions, three poster presentation sessions, and two courses within the main agenda.

We would like to thank all of our colleagues for their participation, the authors for their contributions, and our sponsors for their invaluable support in our growth targets.

Sincerely yours,

Prof. Birol Güvenç, MD
President of Hematology Specialist Association

Prof. Giuseppe Saglio, MD
President of EHOC 2019
President of Eurasian Hematology Oncology Group

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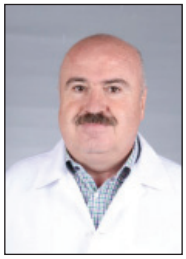

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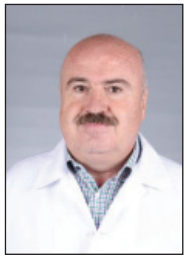

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HEMATOLOGY PROGRAM

8 OCTOBER 2019

12.40–12.50	**OPENING REMARKS – Birol Güvenç and Giuseppe Saglio**

12.50–13.00	**AWARD CEREMONY WITH PRESENCE OF CONSUL GENERAL OF ITALY**	
13.00–13.20	**FRANCESCO LO COCO MEMORIAL LECTURE**	**CHAIR: Giuseppe Saglio**
	Current Treatment of Acute Promyelocytic Leukemia	Miguel Sanz
13.20–15.00	**SESSION I – PRECISION HEMATOLOGY IN MYELOID MALIGNANCIES**	**CHAIRS: Tariq Mughal, Osman Özcebe**
13.20–13.40	Negative Myeloproliferative Neoplasms	Tariq Mughal
13.40–14.00	Precision Hematology in AML	Giovanni Martinelli
14.00–14.20	Precision Hematology in CML	Giuseppe Saglio
14.20–14.40	Precision Hematology in MDS	Mustafa Cetiner
14.40–15.00	Q & A	
15.00–15.30	**COFFEE BREAK – MEET THE PROFESSOR SESSIONS: Guillermo Garcia-Manero / Elias Jabbour**	
15.30–16.50	**SESSION II – HIGHLIGHTS FROM SOHO**	**CHAIRS: Elias Jabbour, Burhan Turgut**
15.30–15.45	SOHO Updates on ALL	Elias Jabbour
15.45–16.00	SOHO Updates on AML	Guillermo Garcia-Manero
16.00–16.15	SOHO Updates on CML	Elias Jabbour
16.15–16.30	SOHO Updates on MDS	Guillermo Garcia-Manero
16.30–16.50	Q & A	
16.50–17.20	**COFFEE BREAK**	
17.20–19.00	**SESSION III – EHOG - RUSSIAN ONCOHEMATOLOGY SOCIETY JOINT SESSION (The Role of Bone Marrow Transplantation in Modern Oncohematology)**	**CHAIRS: Irina Poddubnaya, Larisa Mendeleeva, Pervin Topçuoğlu**
17.20–17.40	The Use of BMT with Malignant Lymphomas. Practical Issues based on St-Petersburg Hematological Center Experience	Natalia Mikhailova
17.40–18.00	BMT Efficacy with Multiple Myelomas. Practical Issues Based on Moscow National Hematological Center Experience	Larisa Mendeleeva, Maxim Soloviev
18.00–18.20	Unrelated Donorship in Russia. Donors' Register (Kirov Hematological Institute)	Maria Alexandrovna Loginova
18.20–18.40	Bone Marrow Allogeneic Transplantation in Oncohematology (Saint-Petersburg Hematology Center Experience)	Ivan Moiseev
18.40–19.00	Q & A	
19.00–20.00	**E-POSTER PRESENTATIONS SESSION I**	**CHAIRS: Vahap Okan, Ozan Salim, İsmet Aydoğdu, Oktay Bilgir**

9 OCTOBER 2019

07.30–08.15	**ORAL PRESENTATIONS – ROOM 1 - Chairs: Rajko Kusec, Gülsüm Özet / ROOM 2 – Chairs: İhsan Karadogan, Atilla Ozkan / ROOM 3 – Chairs: Drew Provan, Ferit Avcu**

08.30–09.45	**SESSION IV – ACUTE LYMPHOID LEUKEMIAS**	**CHAIRS: Dieter Hoelzer, Mustafa Yenerel**
08.30–08.50	Should ALL Treatment Be Driven by MRD Detection	Dieter Hoelzer
08.50–09.10	Current Therapy of Ph Positive ALL	Oliver Ottmann
09.10–09.30	Should the Ph-like ALL Therapy be Different From the Other B ALL? Yes / No	Oliver Ottmann / Dieter Hoelzer
09.30–09.45	Q & A	
09.45–10.15	**COFFEE BREAK**	

HEMATOLOGY PROGRAM

9 OCTOBER 2019

10.15–12.05	**SESSION V – PNH and COAGULATION PROBLEMS**	**CHAIR: Hanan Hamed, Filiz Vural**
10.15–10.35	Hemostasis Changes in PNH	Pierre Toulon
10.35–10.55	Disgnosis and Treatment in PNH	Bulent Antmen
10.55–11.15	Eosinophilia and Mastocytosis: Another Shade of MPN	Hanan Hamed
11.15–11.45	Approaching Consensus in ITP	Drew Provan
11.45–12.05	Q & A	

12.05–12.50	**AMGEN SATELLITE SYMPOSIUM - New Era with Carfilzomib In the Treatment of Relapsed Multiple Myeloma**	**CHAIR: Mehmet Turgut SPEAKER: Sevgi Kalayoglu Besisik**

12.50–13.50	**LUNCH BREAK – MEET THE PROFESSOR SESSIONS: Prasad Adusumilli / Dieter Hoelzer /Paul Szabolcs** **PRACTICAL STATISTICS FOR CLINICIANS: HOW TO CRITICALLY WRITE AND READ CLINICAL TRIALS RESULTS BY ROBERT GALE**

13.50–15.10	**SESSION VI – BEST SELECTED ORAL PRESENTATIONS**	**CHAIRS: Rıdvan Ali, Vera Donnenberg, Orhan Ayyıldız**
13.50–14.00	Best Abstract Presentation (Giuseppe Saglio Prize) –– **Presidential** Analysis of the Progression-Free Survival of CLL Patients Who Received First-Line Bendamustine-Rituximab Therapy Depending on The Elimination Rate of The Minimum Residual Disease and Mutational Status IGHV Genes	Iulia Miroliubova
14.00–14.10	Best Abstract Presentation (Eliezer Rachmilewitz Prize) – **Adult Hematology** Prognostic Implication of Notch 1 Expression Among Adult Patients with Normal Cytogenetic AML	Ghaleb Elyamany
14.10–14.20	Best Abstract Presentation (Francesco Lo Coco Prize) –– **Adult Hematology** A Retrospective Analysis of Peripheral T-Cell Lymphoma Patients: Single Center 'Real-Life' Experience	Murat Ozbalak
14.20–14.30	Best Abstract Presentation (Ekrem Muftuoglu Prize) – **Oncology** Evaluation of Secondary Hypogammaglobulinemia in Patients with Hematologic Malignancy Receiving Ibrutinib Therapy	Serhat Çelik
14.30–14.40	Best Abstract Presentation (Atilla Yalcin Prize) – **Transplant** Is There Any Impact Of Uric Acid Levels During the Peri-Transplant Period on Acute Graft Vs. Disease Incidence and Allotransplant Outcome?	Panayotis Kaloyannidis
14.40–14.50	Best Abstract Presentation (Gularsu Irken Prize) – **Pediatric Hematology** Rituximab Reduction for Pediatric Advanced-Stage Burkitt	Timur Valiev
14.50–15.10	Q & A	

15.10–15.40	**COFFEE BREAK**

15.40–17.20	**SESSION VII – ELN HIGHLIGHTS SESSION**	**CHAIRS: Rudiger Hehlmann, Zafer Gülbaş**
15.40–16.00	2020 ELN Recommandations on CML	Rudiger Hehlmann
16.00–16.20	2020 ELN Recommendations on APL	Miguel Sanz
16.20–16.40	2020 ELN Recommendations on AML	Alan Burnett
16.40–17.00	2020 ELN Recommendations on MDS	Argyris Symeonidis
17.00–17.20	Q & A	

17.20–19.00	**SESSION VIII – CHRONIC MYELOID LEUKEMIA**	**CHAIRS: Naeem Chaundhri, Mehmet Ali Özcan**
17.20–17.40	Choice of TK Inhibitors for CML Therapy	Naeem Chaundhri
17.40–18.00	Molecular Monitoring for CML	Guray Saydam
18.00–18.20	TFR in CML	Carmen Fava
18.20–18.40	Generic TKI's in CML Therapy	Tomasz Sacha
18.40–19.00	Q & A	

19.00–20.00	**E-POSTER PRESENTATIONS SESSION II**	**CHAIRS: Ahmet Öztürk, Tayfur Toptaş, Sinan Dal, Özgür Mehtap, İlhami Kiki**

HEMATOLOGY PROGRAM

10 OCTOBER 2019

07.30–08.15	**ORAL PRESENTATIONS – ROOM 1 – Chairs: Nikolay Tupitsyn, Erdal Kurtoğlu / ROOM 2 – Chairs: Tomasz Sacha, Emin Kaya / ROOM 3 – Chairs: Valeh Huseynov, Salih Aksu**

08.30–09.45	**SESSION IX – ACUTE MYELOID LEUKEMIA**	**CHAIRS: Giovanni Martinelli, Deniz Sargın**
08.30–08.50	Molecular Characterization of AML and Risk Stratification	Giovanni Martinelli
08.50–09.10	Current Therapeutic Options in AML of Young Adults	Mehmet Yılmaz
08.50–09.10	Issues with the Development of FLT3 Inhibitors	Charles Schiffer
09.30–09.45	Q & A	

09.45–10.15	**COFFEE BREAK**

10.15–11.30	**SESSION X – EHOG – AABB JOINT SYMPOSIUM (AABB Highlights in Transfusion Medicine and Cellular Therapies)**	**CHAIRS: Claudia Cohn, Birol Güvenç**
10.15–10.35	Transfusion Support of Patients Following HSCT	Claudia Cohn
10.35–10.55	New Hemostatic Agents in Bleeding and Coagulation Abnormalities	Jose Cancelas
10.55–11.15	Updates on Red Cell Exchange in Hematologic Disorders	Jay Raval
11.15–11.30	Q & A	

11.30–12.15	**BMS SATELLITE SYMPOSIUM – Immunotherapy Data Updates in Treatments Classic Hodgkin Lymphoma**	**CHAIR: Birol Guvenc SPEAKER: Mehmet Ali Ozcan**

12.15–13.15	**LUNCH BREAK – MEET THE PROFESSOR SESSIONS : Alan Burnett / Tariq Mughal / Carmino de Souza PRACTICAL STATISTICS FOR CLINICIANS: HOW TO CRITICALLY WRITE AND READ CLINICAL TRIALS RESULTS BY ROBERT GALE**

13.15–14.00	**NOVARTIS SATELLITE SYMPOSIUM – MF and PV Treatment Journey with Ruxolitinib**	**CHAIR: Ali Unal SPEAKER: Tariq Mughal**

14.00–15.25	**SESSION XI – SPECIAL TOPICS FOR LYMPHOMAS**	**CHAIRS: Carmino de Souza–Burhan Ferhanoglu**
14.00–14.20	How I Treat Relapsed / Refractory DLBCL	Carmino de Souza
14.20–14.40	Non-Hodgkin Lymphoma: Allotransplant Before or After CAR-T Cell Therapy?	Ahmet Elmaagacli
14.40–15.10	How I Treat Early Relapsed Follicular Lymphoma	Elif Birtas Ates
15.10–15.25	Q & A	

15.25–15.55	**COFFEE BREAK**	
15.55–16.25	**ELEZIER RACHMILEWITZ MEMORIAL LECTURE**	**CHAIR: Moshe Mittelman**
	Have We Really Made Progress in the Treatment of MDS?	Charles Schiffer

16.25–18.05	**SESSION XII – EHOG – ISRAEL SOCIETY OF HEMATOLOGY AND TRANSFUSION MEDICINE JOINT SYMPOSIUM**	**CHAIRS: Moshe Mittelman, Ali Ünal**
16.25–16.45	MDS 2019: Pre-MDS States and Diagnosis	Moshe Mittelman
16.45–17.05	Therapeutic Landscape in the treatment of Rel adult ALL	Arnon Nagler
17.05–17.25	The Era of the Haplotransplant	Arnon Nagler
17.25–17.45	Non-Langerhans Histocytosis: the Interplay Between Malignancy and Inflammation	Ofer Shpilberg
17.45–18.05	Q & A	

18.05–19.05	**E-POSTER PRESENTATIONS SESSION III**	**CHAIRS: Oral Nevruz, Ahmet İfran, Sami Kartı, Güven Çetin**

HEMATOLOGY PROGRAM

11 OCTOBER 2019

07.30–08.15	**ORAL PRESENTATIONS – ROOM 1 – Chairs: Ahmed Ibrahim, Fahri Sahin / ROOM 2 – Chairs: Francesco Saglio, Mehmet Sönmez / ROOM 3 – Chairs: Nebosa Andjelkovic, Düzgün Ozatli**

08.30–09.45	**SESSION XIII – CHRONIC LYMPHOCYTIC LEUKEMIAS AND INDOLENT LYMPHOMAS**	**CHAIRS: Robin Foa, Nilgün Sayınalp**
08.30–08.50	Risk Stratification and Treatment of CLL	Robin Foa
08.50–09.10	Molecular Markers in CLL	Panayiotis Panayiotidis
09.10–09.30	New Drugs for CLL	Antonio Cuneo
09.30–09.45	Q & A	

09.45–11.00	**SESSION XIV – EHOG – ASFA JOINT SYMPOSIUM**	**CHAIRS: Robert Weinstein, Osman İlhan**
09.45–10.05	Update on Therapeutic Apheresis Indications	Joseph Schwartz
10.05–10.25	Update on Extracorporeal Photopheresis (ECP)	Jennifer Schneiderman
10:25–10:45	Update on collections for HPC and CAR-T	Anand Padmanabhan
10.45–11.00	Q & A	

11.00–11.30	**COFFEE BREAK**

11.30–12.45	**SESSION XV – MULTIPLE MYELOMA**	**CHAIRS: Angelo Maiolino, Zahit Bolaman**
11.30–11.50	How I Treat Multiple Myeloma	Angelo Maiolino
11.50–12.10	Importance of Minimal Disease Detection in Multiple Myeloma	Evangelos Terpos
12.10–12.30	Impact of Continuous First-Line Therapy in the Treatment of the First Relapse in Multiple Myeloma	Ahmad Ibrahim
12.30–12.45	Q & A	

12.45–13.30	**JNJ SATALLITE SYMPOSIUM – Boosting Outcome in Treatment of Relapsed / Refractory Multiple Myeloma with Monoclonal Antibody**	**CHAIR: Birol Guvenc**
	Importance of Depth and Quality of Response in Multiple Myeloma Treatment	Guray Saydam
	Practice Changing in Treatment of Relapsed / Refractory Multiple Myeloma: Daratumumab Era	Ayse Tulin Tuglular

13.30–14.30	**LUNCH BREAK – MEET THE PROFESSOR SESSIONS : Robin Foa / Robert Weinstein / Albert Donnenberg** **PRACTICAL STATISTICS FOR CLINICIANS: HOW TO CRITICALLY WRITE AND READ CLINICAL TRIALS RESULTS BY ROBERT GALE**

14.30–16.35	**SESSION XVI – STEM CELL TRANSPLANT AND CELLULAR IMMUNO THERAPY**	**CHAIRS: Albert Donnenberg, Hakan Göker**
14.30–14.50	Therapeutic Modulation of The Pleural Effusion Environment: the Next-Gen Immunotherapy	Vera Dannenberg
14.50–15.10	The Secretome of Malignant Effusions: Clues to Targets of Therapy	Albert Donnenberg
15.10–15.30	Are Maintenance Postransplant Therapies Needed?	Khalid Halahleh
15.30–15.50	Will Car T-Cell Therapy Replace Hematopoietic Stem Cells Transplant ?	Francesco Saglio
15.50–16.10	Oral Manifestations of Oral Chronic Graft-Versus-Host Disease	Nathaniel Simon Treister
16.10–16.35	Q & A	

16.35–16.45	**CLOSING**

ONCOLOGY PROGRAM

8 OCTOBER 2019

08.30–12.30	**Cancer Immunotherapy in Lung Cancer Course**	**Başak Oyan Uluç, Berksoy Sahin**

13.20–13.30	**OPENING REMARKS – Berksoy Sahin and Jean-Francois Rossi**

13.30–15.00	**SESSION I – PRECISION AND MOLECULAR ONCOLOGY**	CHAIRS: Uğur Yilmaz
13.30–13.55	Touching Cell Cyle and DNA Repairing: CDK Inhibitors and PARP Inhibitors in Solid Tumors	Uğur Yilmaz
13.55–14.20	How Do Molecular Panels Help Me Make Clinical Decisions About My Patients?	Prasad Adusumilli
14.20–14.45	The Bio-Informatics of Precision Cancer Medicine	Tariq Mughal
14.45–15.00	Q & A	

15.00–15.30	**COFFEE BREAK**

15.30–18.00	**SESSION II – IMMUNE ONCOLOGY (BASIC)**	**CHAIRS: Jean-Francois Rossi, Martin Villalba , Nikolay Tupitsyn, Berksoy Sahin**
15.30–15.55	Precision Immune Medicine in cancer	Jean-Francois Rossi
15.55–16.20	Glycan-specific natural antibodies : from diagnosis to threrapy in cancer	Nikolay Tupitsyn
16.20- 16.45	Natural Killer Cells in Oncology	Martin Villalba
16.45–17.10	Cancer Vaccine : A New Therapeutic Way	Patrick Frayssinet
17.10–17.35	Concluding Remarks in Immune Therapy	Jean-Francois Rossi, Martin Villalba , Nikolay Tupitsyn
17.35–18.00	Q & A	

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08.30–10.00	**SESSION III – IMMUNE ONCOLOGY (CLINIC)**	**CHAIRS: Jean-Francois Rossi, Berksoy Sahin**
08.30–08.55	Allogenic Transplantation as a Model for Immune Therapy in Oncology	Patrice Céballos
08.55–09.20	mAb Biosimilars	Bülent Gümüşel
09.20–09.45	CAR T Therapy for Solid Tumors	Prasad Adusumilli
09.45–10.00	Q & A	

10.00–10.30	**COFFEE BREAK**

10.30–12.00	**SESSION IV – HEAD AND NECK CANCER**	**CHAIRS: Musa Altun, Rasim Meral**
10.30–10.55	HPV-Associated Head/Neck Cancer: New Stagings and New Treatments	Kübra Özkaya Toraman
10.55–11.20	Tumor-Related Factors Warranting Adjuvant Postoperative Therapy in Head and Neck Cancer	Musa Altun
11.20–11.45	p16-Negative Advanced Head and Neck Cancer	Bora Basaran
11.45–12.00	Q & A	

12.00–13.00	**LUNCH BREAK**

13.00–14.30	**SESSION V – NON-SMALL CELL LUNG CANCER**	**CHAIRS: Perran Fulden Yumuk**
13.00–13.25	Sequencing Agents in the Management of EGFR Mutation Positive Non-Small Cell Lung Cancer	Mustafa Erman
13.25–13.50	Management of ALK Non-Small Cell Lung Cancer Through First and Subsequent Lines of Therapy	Fulden Yumuk
13.50–14.15	Immunotherapy in Small and Non-small Cell Lung Cancer; The Role of Immune Checkpoint Inhibitors in Frontline and Beyond Frontline Therapy	Başak Oyan Uluç
14.15–14.30	Q & A	

14.30–15.00	**COFFEE BREAK**

ONCOLOGY PROGRAM

9 OCTOBER 2019

15.00–16.30	SESSION VI – EARLY BREAST CANCER	CHAIRS: Ozlem Er, Hasan Şenol Coşkun
15.00–15.25	Challenging Adjuvant Therapy in HER2+ Breast Cancer: Escalating or De-escalating ?	Çağatay Arslan
15.25–15.50	Evolving Approaches in Systemic Therapy for Triple-Negative Breast Cancer in Neoadjuvant and Adjuvant Settings	Ozlem Er
15.50–16.15	Adjuvant Therapy in ER+ HER2- Breast Cancer: Chemotherapy or Not?	Mehmet Ali Kaplan
16.15–16.30	Q & A	

16.30–18.00	SESSION VII – COLORECTAL CANCER	CHAIR: Mahmut Gümüş
16.30–16.55	Is Shortening the Duration of Adjuvant Treatment is Eligible in Early Staged Colon Cancer?	Ece Esin
16.55–17.20	Is Tumor Sideness, Biomarkers or Molecular Subtype Classification More Predictive for the Treatment of Unresectable Metastatic Colon Cancer?	Gökhan Demir
17.20–17.45	Systemic Therapy for Potentially Resectable Metastatic Rectal Cancer	Dilek Erdem
17.45–18.00	Q & A	

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08.30–11.00	SESSION VIII - NON - COLORECTAL TUMORS	CHAIRS: Şuayib Yalçın, Özlem Er
08.30–08.55	New (neo-)adjuvant Standards of Care in Gastro-esophageal Cancer	Mehmet Artaç
08.55–09.20	What is Changed in the Treatment of Biliary Tract Cancer?	Fatih Köse
09.20–09.45	Has Sorafenib Still Been the Real Winner Against New Generation TKIs and Immune Checkpoint Inhibitors in HCC?	Şahin Laçin
09.45- 10.10	Treatment for recurrent disease following Adjuvant treatment of GIST	Maxim Nikulin
10.10–10.35	Metastatic Well-Differentiated Gastrointestinal Neuroendocrine (Carcinoid) Tumors: Systematic Therapy Options	Alexander Kuzminov
10.35–11.00	Q & A	

11.00–11.30	COFFEE BREAK

11.30–13.00	SESSION IX - ADVANCED / METASTATIC BREAST CANCER	CHAIRS: Berna Öksüzoğlu, Bülent Orhan
11.30–11.55	Optimizing Therapy for ER-Positive Metastatic Breast Cancer	Sema Sezgin Göksu
11.55–12.20	Overcoming Resistance in HER2+ Metastatic Breast Cancer	Sernaz Uzunoğlu
11.20–12.45	Shining Side of the Moon; PARP Inhibitors in Triple Negative Breast Cancer	Ömer Dizdar
12.45–13.00	Q & A	

13.00–14.00	LUNCH BREAK

14.00–16.00	SESSION X – URO-ONCOLOGY	CHAIR: Mustafa Erman
14.00–14.25	Approach to Stage I Testicular Cancer: Who Needs Treatment and Which One?	Ömer Dizdar
14.25–14.50	Treatment of Cisplatin-Ineligible Metastatic Bladder Cancer	Aziz Karaoğlu
14.50–15.15	What is the Role and Best Sequencing of the New Generation Hormonal Agents in the Treatment of Both Hormone Sensitive and Resistant Metastatic Prostate Cancer?	Mustafa Erman
15.15–15.40	Perioperative Systemic Therapy for Localized Renal Cell Carcinoma: To Treat or Not to Treat ?	Çağatay Arslan
15.40–16.00	Q & A	

16.00–17.30	SESSION XI – SKIN CANCER	CHAIRS: İsmail Çelik, Tarkan Yetişyiğit
16.00–16.25	Update on neoadjuvant/adjuvant treatment of melanoma:	Hande Turna
16.25–16.50	Markers for immune checkpoint inhibitor resistance	Selçuk Seber
16.50–17.15	The evolution of metastatic melanoma treatment. What's next?	Dilek Erdem
17.15–17.30	Q & A	

17.30–19.00	SESSION XII – SARCOMA	CHAIR: Berksoy Şahin
17.30–17.55	Molecular and morphological diagnosis in bone and soft tissue tumors	Marco Gambarotti
17.55–18.20	Small round cell tumors	Kıvılcım Eren Erdoğan
18.20–18.45	Can We Ever Have a Specific Treatment for Every 50 Subtypes of Soft Tissue Sarcoma?	Çiğdem Usul Afşar
18.45–19.00	Q & A	

19.00	CLOSING

PEDIATRIC HEMATOLOGY PROGRAM

9 OCTOBER 2019

08.45–09.00		EHOG AND BMT SUBGROUP OF TURKISH PEDIATRIC HEMATOLOGY SOCIETY JOINT MEETING OPENING REMARKS: Namik Ozbek, Bulent Antmen	
09.00–10.30		**SESSION I – BONE MARROW TRANSPLANTATION I**	**CHAIRS: Namik Ozbek, Serap Aksoylar**
09.00–09.30		New Horizons in MUD Transplantation in Childhood	Gulsun Karasu
09.30–10.00		Haplo-Transplant in Pediatric Disease: Now and Future	Francesco Saglio
10.00–10.30	EBMT PDWP BOARD MEETING	BMT Strategies in Relapsed ALL	Atila Tanyeli
10.30–11.00			
10.00–12.00			

10.30–11.00	COFFEE BREAK

11.00–12.30	**SESSION II – BONE MARROW TRANSPLANTATION II**	**CHAIRS: Sema Anak, Gülyüz Öztürk**
11.00–11.30	Stem Cell Transplantations in Congenital Neutropenias	Ekrem Unal
11.30–12.00	BMT in Concert with Solid Organ	Paul Szabolcs
12.00–12.30	The Role of Hematopoietic Stem Cell Transplantation in Pediatric Osteosarcoma and Ewing Tumors	Patrick Leavey

12.30–13.30	LUNCH BREAK

	EBMT PDWP AND BMT SUBGROUP OF TURKISH PEDIATRIC HEMATOLOGY SOCIETY JOINT MEETING OPENING REMARKS: Selim Corbacioglu, Akif Yesilipek, Bulent Antmen

13.30–15.30	**OUTREACH COMMITTEE MEETING**	**CHAIRS: Akif Yesilipek, Lawrence Faulkner, Selim Corbacıoglu**
13.30–14.30	Centers Presentations	
13.30–13.40	BMT Center Organisation	Lawrence Faulkner
13.40–13.50	Transplant Activities, Experience	Valeh Huseynov
13.50–14.00	Transplant Activities, Experience	Dair Nurgaliyev
14.00–14.10	Transplant Activities, Experience	Malek Baassiri
14.10–14.20	Transplant Activities, Experience	Aliya Batol
14.20–14.30	Transplant Activities, Experience	Lalith Parmar
14.30–15.30	**What the PDWP EBMT Outreach Subcommittee Could Do To Facilitate and Support BMT in Eurasian Countries**	
	Round Table: Akif Yesilipek, Lawrence Faulkner, Eugenia Trigoso Arjona,Selim Corbacıoglu	

15.30–16.00	COFFEE BREAK

16.00–19.00	**PDWP EDUCATIONAL MEETING**	**CHAIRS: Selim Corbacioglu, Akif Yesilipek**
16.00 -16.30	Transplant Activity of Turkish Pediatric Stem Cell Transplantation Group	Savaş Kansoy
16.30–17.00	ALL SCT FORUM Study	Christina Peters
17.00–17.30	Haploidentical HSCT in Sickle Cell Disease	Selim Corbacıoglu , Josu De la Fuente
17.30–18.00	Fertility Problems After HSCT C23	Jean-Hugues Dalles
18.00–18.30	Chronic GVHD Follow - Up	Anita Lawitschka
18.30–19.00	CAR-T Cell Therapy in Pediatric Patients	Patrick Schlegel

PEDIATRIC HEMATOLOGY PROGRAM

10 OCTOBER 2019

08.30–10.00	**SESSION III – HEMOPHILIA**	**CHAIRS: Bulent Antmen, Bulent Zulfikar**
08.30–09.00	Extended Half-Life Products in Hemophilia	Can Balkan
09.00–09.30	Nonfactor Therapies for Hemophilia	Kaan Kavaklı
09.30–10.00	Gene Therapy for Hemophilia A and B	Alphan Küpesiz
10.00–10.30	**COFFEE BREAK**	
10.30–11.10	**SESSION IV – PEDIATRIC HEMATOLOGY ONCOLOGY EDUCATION SESSION**	**CHAIRS: Namik Ozbek, Patrick Leavey**
10.30–10.50	Pediatric Hematology/Oncology (PHO) Fellows Education and Training in US	Patrick Leavey
10.50–11.10	Pediatric Hematology/Oncology (PHO) Fellows Education and Training in Turkey	Sabri Kemahli
11.10–12.40	**SESSION V – THALASSEMIA**	**CHAIRS: Zeynep Karakas, Yurdanur Kılınç**
11.10–11.40	Gene Therapy in β-Thalassemia and Sickle Cell Disease	Maria Dimopoulou
11.40–12.10	Upregulating Hemoglobin F Using CRISPR/Cas9 Gene Editing in β-Thalassemia and Sickle Cell Disease	John Chapin
12.10–12.40	Update on Treatment and Management of SCD	
12.40–13.40	**LUNCH BREAK**	
13.40–14.40	**SESSION VI – LEUKEMIA AND THE OTHER MALIGNANCIES**	**CHAIRS: Murat Soker, Tunc Fisgin**
13.40–14.10	Novel Therapy for Relapsed Childhood Acute Lymphoblastic Leukemia	Volkan Hazar
14.10–14.40	Update on HLH Treatment	Şule Ünal
14.40–15.10	**COFFEE BREAK**	
15.10–16.10	**SESSION VII – RED CELLS, THROMBOCYTE AND NEUTROPHILS**	**CHAIRS: Saadet Akarsu**
15.10–15.40	The Approach and Diagonsis of Coombs Negative Hemolytic Anemia	Achilles Iolacson
15.40–16.10	Guideline Developments for Management of Paediatric ITP	Ilgen Sasmaz
16.10	**CLOSING**	

NURSING PROGRAM

8 OCTOBER 2019

11.20–11.30	**OPENING REMARKS – Serpil Vieira and Medine Yilmaz**

11.30–12.00	**SESSION I**	**CHAIRS: Demet Cekdemir, Rose Ellard**
11.30–11.50	Mucositis: Mouth Care Guidance and Support in Cancer and Palliative Care	Barry Quin
11.50–12.00	Q & A	

12.00–13.00	**LUNCH BREAK**

13.00–14.15	**SESSION II**	**CHAIRS: Serpil Vieira, Sule Menziletoglu Yildiz**
13.00–13.20	The Nurse and Patient Partnership in Lymphomas	Erik Aerts
13.20–13.40	Leukaemia	Rose Ellard
13.40–14.00	Managing Multiple Myeloma: What Nurses and Healthcare Professionals Need to Know	Erik Aerts
14.00–14.15	Q & A	

14.15–14.45	**COFFEE BREAK**

14.45–15.35	**SESSION III**	**CHAIRS: Rose Ellard, Ebru Törüner**
14.45–15.00	Therapeutic Use of Apheresis in Haematology/Transplant Setting	Christine Fernandez
15.00–15.15	Apheresis in Paediatric Setting & Nursing Issues	Chrissy Anderson
15.15–15.25	Cell Collections for Gene Therapy: Current Trends	Christine Fernandez & Chrissy Anderson
15.25–15.35	Q & A	

15.35–16.50	**SESSION IV**	**CHAIRS: Christine Fernandez, Fatih Erbey**
15.35–15.55	Therapuetic Communication in Adolescents	Ebru Törüner
15.55–16.15	Palliative care in Paediatrics	Hilda Mekelenkamp
16.15–16.35	Palliative Care & How to Support Nurses	Barry Quin
16.35–16.50	Q & A	

16.50–17.20	**COFFEE BREAK**

17.20–19.00	**SESSION V**	**CHAIRS: Eugenia Trigosa, Medine Yilmaz**
17.20–17.40	Thalassemia and Nursing Considerations	Eugenia Trigosa
17.40–18.00	Transplant Coordinator Role within Paediatrics and Issues	Eugenia Trigosa
18.00–18.20	Fertility Preservation	Fatih Erbey
18.20–18.40	Haplo BMT & Nursing Care	Marjola Gjergji
18.40–19.00	Q & A	

19.00	**CLOSING**

Speaker biographies

Giuseppe Saglio
University of Torino and Ospedale Mauriziano, Torino, Italy

Giuseppe Saglio is a Professor of Internal Medicine and Haematology at the University of Turin. He is Director of the Department of Clinical and Biological Sciences o at the San Luigi University Hospital, Director of the Division of Hematology of the Mauriziano Hospital in Turin and Coordinator of the PhD programme in Molecular Medicine.
Chronic Myeloid Leukemia (CML) is likely to represent in modern medicine the most successful achievement of the so-called targeted therapy and precision medicine. Since the discovery of the Philadelphia chromosome and of its closer association with this specific disease, a continuous flow of biological and clinical research has progressively provided insights on the CML pathogenesis of and on mechanisms leading to its progression to an acute phase, that until two decades ago was the major cause of death for the CML patients. This situation totally changed since the introduction of imatinib, the first tyrosine kinase inhibitor (TKI) introduced in clinical medicine. Several studies indeed suggest that after 10 years from the start of therapy, the OS of the CML patients is almost overlapping that of a control population without leukemia. These results however are not only due to imatinib, but also to other TKIs of second and third generation like nilotinib, dasatinib, bosutinib, radotinib, ponatinib and others. These TKIs are generally used as second or third line treatment in cases (approximately 35-40% of all patients) who are intolerant or resistant to imatinib therapy, but nilotinib, dasatinib and bosutinib have been used and registered also as first line therapy in the attempt to improve the first-line therapy results that can be obtained with imatinib. The decision to change therapy is based on the molecular quantification by quantitative RQ PCR of the amount of the BCR/ABL transcript at specific time points that is corresponding to the amount of the residual disease. The selection of the TKI to be used as first- or second-line therapy is also in many cases established based on the profile of the BCR-ABL mutation present. In other cases, is the toxicity profile of each TKI the factor determinant for the choice. The enormous success of the TKI therapy however should not overshadow the fact that most of them are bound to continue the TKI therapy for the rest of their life. Therefore, the new frontier of the CML therapy is represented by the treatment free remission (TFR) that means that the patient can discontinue the TKI therapy without experiencing a relapse of the disease. This in the next year will certainly represent a new challenge in which the so-called precision medicine will play a major role.

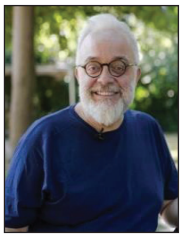
Miguel A. Sanz
Hematology Department, University Hospital La Fe, Valencia, Spain

Miguel Sanz is Researcher Emeritus of the Instituto de Investigación Sanitaria La Fe and Honorary Professor of the Department of Medicine at the University of Valencia. After earning his medical degree at the University of Salamanca in Spain, he was intern, resident and subsequently completed a fellowship in Hematology at the University Hospital La Fe. He was appointed as Head of the Clinical Hematology Section to the University Hospital La Fe in 1977 and then later promoted to Head of the Hematology Department in 2007 as well as Full Professor of Medicine at the University of Valencia. Professor Sanz is chairman of the Spanish PETHEMA Group and leads the working parties of acute myeloid leukemia and infections in neutropenic patients. He is currently a reviewer for numerous high-profile medical journals including all top hematology journals, and has authored more than 550 peer-reviewed papers, numerous book chapters, and in excess of 1100 abstracts at national and international meetings. Professor Sanz has also lectured widely in Europe, North, central and South America, as well as in Middle East and Asia, serving as lecturer at the American Society of Hematology and European Hematology Association meetings in several occasions.

Giovanni Martinelli
IRST IRCCS Cancer Center, Meldola (FC) Italy

Born in Vimercate (MI) on 30/05/1960.
Degree from University of Verona Medical School, 1985.
Postgraduate Specialization School in Hematology, Università of Verona, 1988. Postgraduate Specialization School in Medical Genetics, University of Verona, 1992. From 1994 to 2005, Medical Doctor full-time at Institute of Hematology and Medical Oncology "L. & A. Seràgnoli", University of Bologna (Italy). Professor in Hematology from 01/03/2008. From 2018 Scientific Director at IRST IRCCS Cancer Center, Meldola (FC) Italy.
He has an H-index of 67.
His main research and clinical activity involve the area of acute and chronic myeloid leukemia and myelodysplastic syndromes.
Expertise:
Conduction of several Phase I-II-III clinical trials and biological research projects on AML, LAL, MDS and CML as Principal Investigator. His Research and clinical activities are devoted to translational studies mainly on acute leukemia focusing on the molecular characterization of acute leukemia primary samples using NGS and SNP arrays technologies. Different translational projects are currently integrating genomics data with functional analyses in order to identify novel genetic alterations and to evaluate them as potential targets for innovative therapies.
He has the skills, expertise and authority to lead a team and he has the capacity of using the resources in a flexible way to achieve the project objectives.
He has been involved in different international project: -FP7-HEALTH-2012-INNOVATION-1
Seventh framework programme 2011 Principal Investigator of financed International project: "Next Generation Sequencing platform for targeted Personalized Therapy of Leukemia - NGSPTL". -Coordinator of WP5 of the IMI2 Call topic identifier H2020-JTI-IMI2-2015-06two-stage project named Healthcare Alliance for Resourceful Medicines Offensive against Neoplasms In HematologY (HARMONY) -Partner and WP4 coordinator of the ERA-PER MED call 2018 project:
Synthetic Lethality for Personalized Therapy-based
Stratification In Acute Leukemia

Mustafa Cetiner
Acibadem Maslak Hospital, İstanbul, Turkey



He was born in Kayseri in 1964. He received his MD degree at Ankara University School of Medicine in 1988. He pursued his career at the Department of Hematology in Marmara University Faculty of Medicine as a fellow, an attending physician and an associated professor respectively. He participated in research projects of the Hematopoietic Stem Cell Transplant Program in Northwestern University Robert Lurie Cancer Center**,** Chicago, US as a visiting scholar between 2004 and 2005 for 6 months.
He established Bone Marrow Transplantation Program in Sisli Memorial Hospital and became a director in 2011-2012.
Dr. Cetiner was a professor of the Hematology Department at Koc University School of Medicine between years of 2013 and 2018. He served as a founder and head of the Internal Medicine Department at Koc University School of Medicine in 2015-2018. He worked at the Hematology Department of V.K.V. American Hospital from 2008 to 2019.

He has been working as an official doctor of "United Nations" since 2010.
He is an active member of several national and international medical societies including Turkish Medical Association, the Turkish Society of Hematology, American Society of Hematology, European Hematology Association and MDS Foundation.
He has been a co-chairman of the recognized international meeting "New Trends in Hematology" organized in Istanbul since 2007.
Besides his academic career, Dr. Cetiner remarkably contributes to social responsibility projects. He is among the founders of "Cancer Warriors" in Turkey that is dedicated to providing care and support for cancer patients and their families.
He has an extensive and prominent career as an author. He has published over 50 articles in peer-reviewed scientific national and international journals also 3 books about hematological malignancies. Besides, he has also 3 popular science books titled "To Your Health", "Portraits from the History of Lymphoma" and "The Milestones in the History of Hematology".
He published over 500 columns under the title of "Actual Medicine" in national "Cumhuriyet (Republic) Newspaper" for 10 years till 2017. Currently, he continues to write his columns in weekly "Science and Technology Magazine".
He is currently working at the Hematology Department of Acibadem Maslak Hospital.

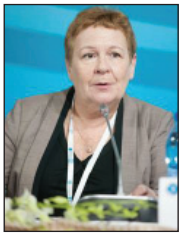
Guillermo Garcia-Manero
University of Texas MD Anderson Cancer Center, Houston, TX, USA

Dr. Guillermo Garcia-Manero is the Dr. Kenneth B. McCredie Chair in Clinical Leukemia Research in the Department of Leukemia at the University of Texas MD Anderson Cancer Center.
He also serves as the Chief of the Section of Myelodysplastic Syndromes, Vice Chairman for Translational Research, Leader of the AML/MDS Moon Shot Program and Program Director of the Leukemia Fellowship Program (September 2019). He recently was elected as Chair-elect of the Faculty Senate of the University of Texas MD Anderson Cancer Center, which also starts in September 2019. Dr. Garcia-Manero was born in Spain and received his medical degree and training at the University of Zaragoza in Spain and at the Royal Free Hospital in London, UK. From 19931996, he performed his internship and residency in Internal Medicine at Thomas Jefferson University Hospital in Philadelphia, PA. He then continued his training with a fellowship in Hematology and Medical Oncology at the Cardeza Foundation for Hematology Research, Sidney Kimmel Cancer Center, also at Thomas Jefferson University Hospital, where he served as chief fellow. In 1999, he became Assistant Professor in the Department of Leukemia at the University of Texas MD Anderson Cancer Center where he has remained for the rest of his academic career. Dr. Garcia-Manero focuses on the understanding the cellular and molecular biology of MDS and AML with an aim to improve therapeutic options for patients with these disorders. His work has been funded by NIH, DoD, LLS, CPRIT, and the MDS/AML Moon Shot project. He has coauthored over 682 manuscripts. His last H-index is 119 and his i10-Index is 630 with over 58,000 citations to his work. Currently, he is PI or Co-PI on over 25 active clinical trials focusing on AML and MDS. He directs what is likely the largest single institution unit for patients with MDS in the world, with over 400 patients referred annually, and maintains one of the busiest clinics at MD Anderson. The Section of MDS is comprised of leukemia faculty dedicated to care for patients with MDS and two research laboratories directed by Dr. Colla and Dr. Wei. In addition, the section coordinates the work of over 15 research nurses. Dr. Garcia-Manero has received a number of significant awards, such as The Otis W. and Pearl L. Walters Faculty Achievement Award in Clinical Research and the Emil J. Freireich Award for Excellence in Translational Research at MD Anderson. He has also been recognized as one of the Best Doctors in America each year since 2007. He has trained over 100 fellows and postdoctoral fellows and has been a speaker at multiple national and international forums.

Irina Poddubnaya
Russian Academy of Sciens, Russia

Ph. D., Professor, Vice-rector for Educational Work and International Cooperation,
Heard of Oncology and Palliative Medicine Chair, Russian Medical Academy for Continual Professional Education of Russian Ministry of Health.
Since 1974 she works in Russian Medical Academy for Continual Professional Education (RMACPE) as assistant lecturer, associate professor, professor, and since 1989-Heard of department. In 2003 she was appointed as a vice-rector
RMACPE. Prof. Poddubnaya since 2005 is a corresponding Member and since 2014 is Academician of Russian Academy of Science.
Her main sphere of scientific interests includes all aspects of diagnosis and treatment of malignant lymphoproliferative disorders and different forms of solid tumors; her activities include scientific clinical research, teaching and lecturing, as well as developing international scientific cooperation projects.
In 1994 she received the ESSO Sekiyu Kabushiki Kaisha Research grant (Japan) for her Research "Study of different features of nodal and extra-nodal non-Hodgkin adult lymphomas and development of effective treatment". In 2002 prof. Poddubnaya was awarded as a Honorary Educational Worker of Russia.
In 1999-2002 she was a member of Annal Oncology Editorial Board as a member of the ESMO Publishing Working Group. She is Editor-in- Chief of quarterly Russian journal " Contemporary Oncology" since 1999. 2012-2016 she was Editor-in-Chief of Russian edition of *Journal of Clinical Oncology* (ASCO).She is the organizer and chair of annual Russian Conference with International Participation "Malignant Lymphomas". Since 2011 she is president of Russian Society of Oncohematologists".
Prof. Poddubnaya actively participates in numerous International and Russian clinical trials as principal investigator or co- investigator. She is author more than 550 articles, 8 monographies, chapters in manuals. Since 2012 she is editor-in-chief of Russian National Clinical Recommendations on Diagnostics and Treatment of Lymphoproliferative Diseases (in 2018 the 4th edition).

Natalia Mikhailova
Raisa Gorbacheva Memorial Research Institute, Saint Petersburg – Russia
Pavlov First St. Petersburg State Medical University, St. Petersburg, Russia



PhD, Head of oncology department of Raisa Gorbacheva memorial Research Institute for Pediatric Oncology, Hematology and Transplantation, Associate Professor, Department of Hematology, Transfusiology and Transplantation, Faculty of Postgraduate Education of Pavlov First St. Petersburg State Medical University.
She graduated from Leningrad Medical Institute in 1979, and then studied in residency in internal medicine. In 1986, she also completed residency in clinical oncology. For 10 years, she worked as the head of the bone marrow transplantation department at the Oncology Research Institute named after prof. N. Petrov in St. Petersburg. Since 1998, she has been working at Pavlov First SPbSMU under the leadership of professor B. Afanasyev. She is engaged in clinical, educational and scientific work. Her main research interests are related to the development of new methods for overcoming chemoresistance in patients with various malignant lymphomas, including bone marrow transplantation and immunotherapy. N.Mikhailova is the coauthor of more than 100 scientific publications.

Larisa Mendeleeva
National Research Center for Hematology

Deputy Director General of National Research Center for Hematology, Head of the high dose chemotherapy of paraproteinemic
Hemoblastosis department. Clinical and scientific activities focused on the development and implementation of the intensive transplantation methods for oncohematological patients' treatment.
The priority area is studying of pathogenetic characteristics, clinical course and up to date multiple myeloma treatment methods, including early intensification and high dose transplant consolidation. Disease biological features are also investigated based on molecular-biological researches. Moreover, therapy effectiveness is analysing, including survival rate of patients, significance of minimal residual disease, cytogenetic abnormalities, histological and immunohistochemical tests. Modern visualization methods are being introduced. Under the Professor Mendeleeva leadership, population research (Register) is done among multiple myeloma patients in different regions of Russian Federation. She is Russian bone marrow transplantation register's coordinator.
Takes part in numerous new drugs clinical trials. More than 350 publications are published in Russian and foreign journals with her participation. She is a co-author of the national clinical recommendations of myeloma diagnosis and treatment.
Member of the National Hematology Society, board member of Russian professional oncohematologic association. Member of editorial board of *Hematology and Transfusiology* journal, member of editorial board of *Oncohematology* and *Therapeutic archive* journals.

Solovev Maxim
National Research Center for Hematology, Russian Federation, Moscow

MD, PhD, Head of the Department of Intensive High-Dose Chemotherapy of Paraproteinemic Hemoblastosis, National Research Center for Hematology, Russian Federation, Moscow.
The scientific and clinical activities of Dr. Solovev are devoted to the study of various aspects of multiple myeloma. He is the coordinator of a multicenter prospective observational registration study to assess the epidemiological characteristics and clinical features of MM in Russia.
Dr. Solovev takes an active part in international clinical trials on the effectiveness of the therapeutic effects of innovative drugs in refractory multiple myeloma.
The main focus of his scientific and clinical activities is the study of various aspects of multiple myeloma, including stem cell transplantation.

Mariia Loginova
Federal Medical Biological Agency of Russia

Education:
Biological faculty, qualification – engineer, specialty – biotechnology
2008 PhD of biological science.
Work experience:
2004–2005 Pharmaceutical Company: ALSI Pharma
Position: quality controlling master; Function: control of intermediate and finished products in the preparation of tableted forms of pharmaceutical products
2005–2008 Federal State Institution: 48 Central Research Institute of the Ministry of Defence of the Russian Federation
Position: laboratory assistant, researcher; Function: work with DNA-samples: polymerase chain reaction, gel electrophoresis in agarose and polyacrylamide gels, choice of primers, STR- and VNTR-analysis; HLA-typing on SSP (sequence specific primers) technology; DNA sequencing
2008–2018 Russian medical scientific and production center Rosplasma of Federal Medical Biological Agency of Russia
Position: head of the Department of hematopoietic stem cells donation; Function: recruiting potential donors of hematopoietic stem cells, HLA-typing, general management of the department, development new technologies in immunogenetics (including NGS - next generation sequence), identification of new HLA-alleles
2019–present Kirov scientific-research institute of hematology and blood transfusion of Federal Medical Biological Agency of Russia
Position: head of Research Laboratory of applied immunogenetics; Function: HLA-typing, general management of the department, development new technologies in immunogenetics (including NGS - next generation sequence), identification of new HLA-alleles, analysis of chimerism after allogenic stem cell transplantation

Drew Provan
The London School of Medicine and Dentistry, London, UK

Drew Provan is Emeritus Reader in Autoimmune Haematology at Barts and The London School of Medicine and Dentistry in London, UK. He studied molecular genetics at Leicester University, UK before completing his medical degree. After junior medical posts in the UK, Dr Provan undertook research at The Dana–Farber Cancer Institute in Boston, USA on an American Travelling Fellowship awarded by the UK's Medical Research Council. He subsequently became a Consultant Haematologist at Southampton University NHS Trust before assuming his current position. Dr Provan's research interests include immune thrombocytopenia (ITP), neutropenia and haemolytic anaemia. He established the UK Adult ITP Registry, a clinical and laboratory database of patients with ITP for symptom recording, genetic analysis and remote monitoring, with the hope of establishing the underlying mechanisms leading to autoantibody production and identifying treatment response genes and surrogate markers. Along with international colleagues, Dr Provan published the consensus guidelines for the diagnosis and management of ITP in children and adults which is being updated and will be submitted early August 2019. He has written numerous peer-reviewed papers and book chapters, and has authored several medical books including Molecular Hematology, Oxford Handbook of Clinical Haematology, Oxford Handbook of Clinical and Laboratory Investigation, and ABC of Clinical Haematology.

Dieter Hoelzer
Internal Medicine University of Frankfurt, Germany

Dieter Hoelzer is Professor of Medicine and Hematology. His main research is Acute Leukemias. He founded the German Adult ALL Study Group (GMALL) which so far conducted 7 multicenter studies in >145 participating hospitals, where more than 7000 patients were treated.
Prof. Hoelzer was one of the five founders and President of the European Hematology Association (EHA), currently Vice President of the European and German Competence Network Leukemias and he also founded the European Working Group on Adult Acute Lymphoblastic Leukemia (EWALL).
He currently chairs the Medical Advisory Board of the German Carreras Leukemia Foundation. Recently he was also the President of the Society for Hemato Oncology (SOHO). He is a member of the Medical Council and the Foundation Board of the DKMS (Deutsche Knochenmark Spender Datei).
Prof. Hoelzer received several awards for cancer research and therapy including those of the German Cancer Society, the "Deutsche Krebshilfe", the Johann-GeorgZimmermann-Price, the San Salvatore Award and the European Leukemia Network Merit Award. He is a honorary member of

the Hematological Societies of Austria, Hungary and Germany (DGHO) and received the doctor honoris causa from the University of Athens.
Prof. Hoelzer is author or co-author of more than 800 peer-reviewed publications and co-author of international text books, such as Oxford textbook of Oncology and Harrison´s principles of Internal Medicine 2018.

Oliver Ottmann
Cardiff University School of Medicine, Cardiff, UK

Oliver Ottmann is Professor and Head of Haematology at Cardiff University School of Medicine and Co-Lead of the Cardiff Experimental Cancer Medicine Centre (ECMC). Before taking up his current position in 2015, he was Head of the Division of Molecular Therapeutics at the Goethe University in Frankfurt, Germany and Endowed Professor for Molecular Therapy Research of the Deutsche Jose Carreras Leukemia Foundation.
Professor Ottmann's scientific interests focus on malignant hematology with a particular emphasis on clinical trials, translational research including biomarker identification and validation, minimal residual disease, pre-clinical drug development as well as mechanisms of leukaemogenesis and drug resistance. He is internationally recognized for his expertise in the therapy for BCR-ABL positive leukemias and as an early phase clinical trialist. Prof. Ottmann is a member of many international professional societies including the European Hematology Association (EHA), the European Working Group for Adult ALL (EWALL) and the American Society for Hematology (ASH).

Pierre Toulon,
Pasteur University Hospital, Nice, France

Associate Professor of Hematology, Côte d'Azur University, Nice, France
Head, Hemostasis and Thrombosis Laboratory, Pasteur University Hospital, Nice, France
Pierre Toulon has more than 30 years' experience in hemostasis laboratory development and management. He received his Pharmaceutical degree from the Paris XI University in 1987 and completed his PhD at Paris V University in the field of hemostasis and thrombosis in 1991. He was the director of the Laboratory of hemostasis and thrombosis at Cochin University Hospital in Paris, France and Associate Professor of Hematology at the Paris V University between 1987 and 2003, before taking his current position at Nice University Hospital since 2003. Dr Pierre Toulon is a member of many international and national societies including the World Federation of Hemophilia (vice-chair, Laboratory Science Committee), the American Society of Hematology, the American Heart Association (FAHA, Council on Atherosclerosis, Thrombosis and Vascular Biology), the International Society on Thrombosis and Haemostasis, the International Society for Laboratory Hematology, the French Society of Hematology and the GFHT (French Working Group on Thrombosis and Hemostasis).

Alan Burnett
The Paul O'Gorman Leukaemia Unit, Glasgow University, Glasgow, UK

Dr Alan Burnett was trained at Glasgow University in the UK. He did postgraduate research in the Ben May Laboratory for Cancer Research, University of Chicago, IL, USA, and returned to Glasgow, where he established the Stem Cell Programme, including the first CR1 autografts in acute myeloid leukaemia (AML). He was appointed chair of the Medical Research Council (MRC) Adult Leukaemia Working Party in 1989 and has acted as a coordinator of the MRC AML 10, 11, 12, 14, 15, 16, and 17 trials. He was Professor and head of the Department of Haematology at the University of Wales College of Medicine (now Cardiff University) in 1992–2014. In 2002, the National Cancer Research Institute was established in the UK and Dr Burnett was appointed chair of its Haematological Oncology Study Group.
Dr Burnett's main research interest is the development of treatments for AML. He has published more than 300 papers and served on numerous advisory committees, and is past president of the British Society for Haematology and chair of the UK National Training Programme. He was elected as a Fellow of the Academy of Medical Sciences in 2002, was awarded the Gold Medal of the British Society for Haematology in 2004, was appointed as an MBE in the Queen's Birthday Honours for services to medicine in 2008, and received the Ham-Wasserman Lecture award from the American Society of Hematology in 2012. He was Global Lead for Myeloid Diseases for CTI Biopharma, Seattle 2015–2017.

Naeem Arshad Chaudhri
College of Medicine, Alfaisal University Director, Research Unit, Oncology Centre Consultant, Adult Hematology/HSCT King Faisal Specialist Hospital & Research Centre Riyadh, Saudi Arabia

Dr. Chaudhri is a Consultant in Hematology and Hematopoietic Stem Cell Transplantation at KFSH&RC. He is board certified in Internal Medicine, Medical Oncology and Hematology from American Board of Internal Medicine and he completed his fellowship in Hematology and Medical Oncology in 1995 at Lombardi Cancer Center, Georgetown University Hospital, Washington D. C. He joined King Faisal Specialist Hospital and Research Centre in 1996. KFSH&RC is the major tertiary care referral centre in Saudi Arabia and Middle East with Oncology Centre being accredited by the World Health Organization (WHO) as a Collaborating Centre for Cancer Prevention and Control.
His main interest is Malignant Hematology, specifically Acute and Chronic Leukemia as well as Hematopoietic Stem Cell Transplant.
Dr. Chaudhri is also the Director/Head of Research Unit overseeing clinical research in the Oncology Centre at KFSH&RC. He is the principal investigator of the South West Oncology Group (SWOG) for KFSH&RC and principal investigator of numerous ongoing clinical trials. He is an Associate Editor-in-chief of Annals of Saudi Medicine and an Editorial Board of other journals. He has around 130-140 publications and abstracts in peer-reviewed journals. At the same time, Dr. Chaudhri is the Congress Chairman of the annual conference of the Critical Reviews in Hematological Malignancies in Riyadh, Saudi Arabia and also a member of organizing and scientific committees of numerous national and international meetings. He is invited speaker on national and international scientific meetings.

Giray Saydam
Dept. of Hematology, Ege University Hospital, Izmir Turkey

He worked as a resident in Internal Medicine Department of Ege University Faculty of Medicine from November 30th, 1993 to 24th May, 1999. He finished his hematology fellowship in Hematology Unit, Ege University Medical School. He worked as hematologists between 2001 and 2003 at the same clinic and then he moved to CINJ New Jersey as an postdoctoral fellow in Dr. Bertino's laboratory.
Dr Saydam has been working in hematology field since 1997. He started to work in lab on mainly phosphatase and kinase systems in leukemias at the same time. He did his hematology fellowshipn in Ege University between 1998 and 2000. He moved to Cancer Institute of New Jersey (CINJ) in 2003 and worked in CINJ between 2003 and 2004. He worked in CINJ under the mentorship of DR Joseph R. Bertino and main research field was new drug development, signaling systems in cancer. He was mainly involved in preclinical studies of Aplidin. He came back to home country in 2004 and he became associate prof of medicine in 2005. He established a molecular study lab in his own center to perform in vitro studies. He

became chair of Molecular and Cytogenetics Subcommittee of Turkish Hematology Association in 2006 and afterwards, we have been working on molecular monitorization and standardization in CML (as part of EUTOS project), clonality analysis for hematopoietic and lymphoid malignancies and establishing regional reference labs for molecular diagnosis and follow-up of hematological malignancies.
His main research topic is CML and CMPD.

Tomasz Sacha
Jagiellonian University Hospital, Krakow, Poland

Graduated from the Medical Academy in Kraków in 1992. During his studies, he worked actively in the research team at the Department of Internal Medicine in Kraków and won twice the prize of the Students' Scientific Society competition for the best scientific project. He worked as an assistant in the Haematology Department at the Jagiellonian University in Kraków after initial specialization in internal medicine. He specialized further in haematology after several pieces of training in Basel, Genoa and Turin, and became a lecturer and professor at the Jagiellonian University in Kraków. He received his PhD for his work on molecular diagnostics of Chronic Myeloid Leukemia (CML). In 2008, he completed his specialization in laboratory diagnostics and, in 2013, he habilitated at the Jagiellonian University. Dr Sacha established a National Molecular Reference Laboratory for quantitative BCR/ABL analysis and is responsible for the standardization of this procedure in Polish Molecular Laboratories. In 2002 he contributed to the organization of Polish Advocacy Group of patients suffering from chronic myeloid leukaemia. For his activity, he was awarded the prize: "Service for Life Award" and became an Honorary Member No 1 of this Society.
Since 2013, he is a president of the Molecular Hematology Section of the Polish Society of Human Genetics, and since 2017 he is the president of Chronic Myeloid Leukemia Section of the Polish Adult Leukemia Group, and since May 2019 he is the head of The Chair and Department of Hematology in Jagiellonian University Hospital. He has an extensive clinical experience in the use of tyrosine kinase inhibitors and in the field of molecular monitoring of chronic myeloproliferative neoplasms. He is also interested in the clinical research of myeloproliferative neoplasms aiming at eliminating the leukemic stem cells.

Valeh Huseynov
Therapeutic Clinic of Azerbaijan Medical University. Azerbaijan Baku

Thalassemia Center.
Birth date: 01.05.1976.
Place: Azerbaijan.
Generation: Azerbaycan.
Education:

1992–1998	Azerbaijan Medical University.
1998–1999	Azerbaijan Medical University, Oncology Hospital, Oncology – Hematologist.
1999	Oncology course on rehabilitation, Kazakhstan, Almaty.
2002	Rehabilitation course on hematology and bone marrow transplantation. Sample education and research Hospital, Turkey, Ankara.
2002	Regional Blood Banking Implementation Course, Turkey.
2005	WHO training course. Quality management in the blood transfusion service.
2015	Course of Quality Standards of Cellular Therapy Products in Current Use.
1999–2001	Republic Oncology Center, Oncologist-Hematologist, Junior researcher, Kazakhstan, Almaty.
2005	WHO course. Quality control during bleeding, Baku.
2010	Course at the Medical University of Vienna. Vyana, Avstriya, Hematologiya və Sümük iliyi transplantasiyası.
2013	Hematology and Bone Marrow Transplantation Course. Memorial Hospital, Istanbul, Turkey.
2014	Ankara Univ., Department of Hematology, Bone Marrow Transplant Unit, Ankara, Turkey.
2016	Oncological hematology and bone marrow transplantation. Tennessee University, Memphis, USA.

Work experience:

1998–1999	City Oncology Dispensary, chemical therapy. Internship. Azerbaijan Baku.
1999–2000	Republic Oncology Center, Oncologist-Hematologist. Small scientific worker in Kazakhstan, Almaty.
2000–2002	Institute of Hematology and Transfusiology, Hematologist named after B. Eivazov. Scientist. Azerbaijan Baku.
2001–2015	Central Clinical Hospital. Hematologist. Azerbaijan Baku.
2003–2009	Head of Hematology and Oncology Department and Blood Bank Central Clinic. Azerbaijan Baku.
2009–2012	Head of the Therapy Center. Central Clinic. Azerbaijan Baku.
2013–present	Head of Department of Hematology at Educational-Therapeutic Clinic of Azerbaijan Medical University. Azerbaijan Baku.
2017–present	Director of the Thalassemia Center.

Member of societies:
European Hematology Society (EHA)
American Hematology Society (ASH)
Chairman of the Society of Hematology Professionals of Azerbaijan.

Claudia S. Cohn
The University of Minnesota, in Minneapolis, MN, USA

Dr. Cohn earned her PhD in Immunology and Infectious Diseases from the Johns Hopkins University (currently the Bloomberg School of Public Health) and subsequently earned her MD at Louisiana State University. After finishing her Transfusion Medicine fellowship at University of California, San Francisco, Dr. Cohn joined the faculty at the University of Minnesota, in Minneapolis, where she is Medical Director of the Blood Bank, Associate Medical Director of the HLA lab and Associate Head of Labs. Dr. Cohn's major interests include hemovigilance, transfusion support for umbilical cord transplants, blood safety and pathogen-inactivated blood components and appropriate use of blood components. Dr. Cohn is the current editor in chief of the next edition of the AABB Technical Manual, chairs the AABB Clinical Transfusion Medicine Committee and has been an active member of the Transfusion Transmitted Disease Committee.

Jose Cancelas
University of Cincinnati College of Medicine, Cincinati, USA

MD, PhD is Professor of Pediatrics at the University of Cincinnati College of Medicine and leader of the Stem Cell group of the Cancer & Blood Diseases Institute of Cincinnati Children's Hospital Medical Center. He is also the Director of Hoxworth Blood Center and holds the Beatrice C. Lampkin Endowment for Stem Cell and Hematotherapy Research.
Dr. Cancelas has published over 150 peer-reviewed manuscripts in the areas of hematopoiesis and transfusion/cell therapies. His laboratory is funded by the NIH, US DoD and different private foundations and corporations. Dr. Cancelas has trained over 40 MD, PhD and MD, PhD professionals. His basic biology laboratory has contributed to the elucidation of the cellular and molecular mechanisms

of hematopoietic stem cell, granulocyte progenitor activity and platelet survival through the Rho family of GTPases in health and leukemia and provided the basis for understanding the physiological cell-autonomous and microenvironment/cytokine dependent mechanisms that control HSC activity in the BM microenvironment. In normal and pathological hematopoiesis, his group defined the mechanisms that control oncogenic tyrosine kinase signals dependent transformation in leukemic progenitors through intrinsic and microenvironment-dependent signaling. His transfusion medicine group is trying to identify novel methods to preserve red cell and platelet potency upon long-term storage and generate alternative blood products to cover unmet clinical needs.

Carmino Antonio De Souza
Brazilian Hematology and Hemotherapy Association

Graduated in Medicine in 1975, Medical Residency in Internal Medicine and Hematology and Hemotherapy 1976–1979, PhD in 1987, Free Professor in 1996 and Full Professor in 2001 of the Department of Internal Medicine of the Faculty of Medical Sciences - University of Campinas – São Paulo State - Brazil. He completed postdoctoral studies at the Department of Hematology, San Martino Hospital, University of Genoa, Italy, in 19971998. Oncohematologist, working in the Malignant Lymphomas, Chronic Myeloid Leukemia and Bone Marrow Transplantation. He has about of 350 published papers, mainly in English and Portuguese, more than 1200 abstracts in national and international congresses; 25 chapters of scientific books and 45 approved theses of master and doctorate degrees. H index 54 and Hi10 index 254 (Google Scholar July 2019). He is member of the Hematology, Hemotherapy and Cell Therapy Brazilian Association, the American Society of Hematology (ASH), the European Association of Hematology (EHA), the European Bone Marrow Transplant Group (EBMT) and founder member of LALNET (Latin America Leukemia Net) and AIBE (Brazilian Italy Association of Hematology). Head of the Hematology and Hemotherapy Center 1985–1993 and 2006–2011. São Paulo State Minister of Health 1993–1994. Scientific Director of Brazilian Hematology and Hemotherapy Association (ABHH) 2005–2009 and President of Brazilian Hematology and Hemotherapy Association (ABHH) 2009–2013.

Charles A. Schiffer
Wayne State University School of Medicine and the Karmanos Cancer Institute in Detroit

Charles A. Schiffer, MD, is Professor of Medicine and Oncology and the Joseph Dresner Chair for Hematologic Malignancies at Wayne State University School of Medicine and the Karmanos Cancer Institute in Detroit, Michigan. He is the director of the Leukemia/Lymphoma Multidisciplinary Program.
Dr. Schiffer earned his BA *cum laude* at Brandeis University and his M.D. at New York University School of Medicine. He completed his internship, residency, and chief residency in Internal Medicine at Bellevue Hospital under the auspices of New York University School of Medicine and had subsequent training and positions at the Baltimore Cancer Research Institute, National Cancer Institute and the University of Maryland School of Medicine, where he served as Chief of the Division of Hematology. He has also served as Chief of the Division of Hematology/Oncology and Director of Clinical Research at the Karmanos Cancer Institute.
Dr. Schiffer has authored and co-authored more than 310 articles and 75 book chapters on topics concerning the treatment of leukemia in adults, platelet transfusion, and granulocyte transfusion therapy, among others. He has served on the Editorial Boards for Blood, the Journal of Clinical Oncology, International Journal of Hematology, Transfusion Medicine Reviews and Transfusion, and reviews articles for multiple journals. Committee memberships have included Chairman of the Leukemia Committee of the Cancer and Leukemia Group B, Chairman of the Food and Drug Administration Oncologic Drug Advisory Committee, and grant reviews for the NCI, ASH, DOD, ASCO and Leukemia/Lymphoma Society of America. Dr. Schiffer has been named among Castle Connelly's "Best Doctors in America," and Newsweek's "Best Cancer Specialists in the US." In 2006, he received the Dr. John J. Kenney Award from the Leukemia/Lymphoma Society of America and the Celgene Award for Career Achievement in Hematology. He was recently inducted into the Academy of Scholars of Wayne State University, the highest recognition accorded to academic faculty at the University.

Ali Ünal
Erciyes University, Turkey

He is working at Erciyes University Haematology-Oncology department and Bone Marrow Transplantation Center, in Kayseri, Turkey.
He received his MD degree at Erciyes University Medical School in Kayseri. He started his postgraduate training in the department of Haematology at Ankara University Ibni Sina Hospital and subsequently completed at the London University Royal Postgraduate School of Medicine Hammersmith Hospital.
His scientific training in Bone Marrow transplantation and cancer immunotherapy was gained at the Hebrew University Hadassah Medical School Bone Marrow Transplantation (Jerusalem, Israel).
Ali Unal's main areas of research interests focus on: Haematological malignancy, Bone marrow transplantation, lymphoma, stem cell transplantation and therapeutic apheresis. His clinical research activities are mainly in the area of the lymphoma, leukaemia and tumour immunotherapy.
He was the president of Turkish Apheresis Society and member of, and Co-President of WAA 2012 Congress. He is member of National Haematology Association, European Society for Medical Oncology, American Society for Hematology and European Haematology Association.
He is serving on the editorial board of Turkish Haematology-Oncology Journal. He has published more than 200 scientific articles in international and national journals, peer-reviewed papers, review articles, book chapters, congress abstracts and oral presentations.

Ahmad Ibrahim
National Lebanese University

He is a full Professor of Medicine, Hematology/Oncology and Physiological Sciences at the Faculty of Medicine of the National Lebanese University, a Professor of Medicine at the Arab University of Beirut, an Associate Professor of Oncology at University of Paris XI, and Clinical Associate-Department of Internal Medicine at the American University of Beirut.
He graduated, from the University of Paris VII-School of Medicine in 1987. Then, he pursued a fellowship in Hematology/Oncology, Immunology (HLA Lab, Professor Jean Dausset, Noble price of Medicine), and Bone Marrow Transplantation at the University of Paris; then, a post fellowship in the department Bone Marrow Transplantation at Fred Hutchinson Cancer Center, Seattle, USA (Professor E.D. Thomas, Noble price of Medicine).
Doctor Ibrahim was appointed in 1993 as a full-time Attending Physician/Associate professor in the Department of Hematology and Bone Marrow Transplantation at the Institute Gustave Roussy (IGR)-Villejuif/University of Paris XI. In 1997, he moved to Lebanon where he established the first Bone Marrow Transplantation Program at Makassed Hospital-Beirut which was affiliated with IGR/University of Paris XI in a French-Lebanese cooperation. Since 1997, Dr. Ibrahim has been the head of the Division of Hematology/Oncology and the Director of the Bone Marrow Transplantation Program at Makassed Hospital. Since 2004, he has been appointed associate director of research for PhD Programs at the Faculty of Pharmacy/University Paris V. Since 2012. He has been board member of Masters Programs in stem

cell engineering and applications at the faculty of Sciences of the National Lebanese University. In 2018, Dr. Ibrahim was the coordinator of the guidelines for Hematological Diseases established for the Ministry of Public Health in Lebanon in cooperation of UNDP. Dr. Ibrahim is currently in advisor of International Clinical Practice Guidelines on the Treatment and Prophylaxis of Venous Thromboembolism in Patients with Cancer (ITAC-CME CPGS).

Dr. Ibrahim is actively involved in research particularly in the fields of hematological malignancies and hematopoietic stem cell transplantation. In 1993, he was nominated a core member of the European Organization for Research and Treatment of Cancer (EORTC)-Leukemias Cooperative Groups. In 1996, he was elected member of the French College of Hematology. Since 2009, he has been member of the Board of Directors of the Eastern Mediterranean Group for Blood and Bone Marrow Transplantation (EMBMT). He is member of the American Society of Hematology (ASH), European School of Medical Oncology (ESMO), European Hematology Association (EHA), European Group for Blood and Marrow Transplantation/Acute Leukemias and Lymphoma working parties (EBMT), and the American Society for Blood and Marrow Transplantation (ASBMT).

Dr. Ibrahim is currently the President of the Lebanese Society of Hematology and Blood Transfusion, Key partner of the ASH and EHA.

Dr. Ibrahim has taken an active role in the medical community-participating in numerous scientific meetings. He has authored and co-authored more than 300 medical publications and books chapters. He is also co-editor of a book in Hematology (edited in Paris-Maloine Publisher -1992).

In 1992, he received the Research Award of the Medical School of the University of Paris VII. In 1993, he received the award of the French League Against Cancer. In 2013, Dr. Ibrahim was awarded by the Lebanese Ministry of Health for his achievement in the field of hematopoietic stem cell transplantation in Lebanon. In 2018, he received the award of achievement from the Pan Arab Hematology Association/EHA in Cairo, Egypt.

Francesco Saglio

Regina Margherita Children's Hospital, Torino, Italy

Education:

2001–2007	MD Università degli Studi di Torino (Italy)
2009–2014	Pediatrics Università degli Studi di Torino (Italy)
2011–2012	Post-doctoral Fellowship Baylor College of Medicine, TX, US
2014–2018	PhD Biomedical Sciences & Oncology Università degli Studi di Torino (Italy)

Work Experience:

2014–2015	Part-time Attending Physician Pediatric Emergency Room, AOU Città della Salute e della Scienza di Torino, Turin, Italy
2015–2017	Attending Physician Pediatric Onco-Hematology, Cell Therapy and Stem Cell Transplantation Unit, AOU Città della Salute e della Scienza di Torino, Turin, Italy
2017–present	Full-time position Attending Physician Pediatric Onco-Hematology, Cell Therapy and Stem Cell Transplantation Unit, AOU Città della Salute e della Scienza di Torino, Turin, Italy

Main areas of interest:

Main areas of interest are the immunological aspects of hematopoietic stem cell transplantation in the pediatric population especially in relation to the opportunity to generate virus and leukemia directed cytotoxic T cell lines to be used in adoptive cell therapy protocols. Experience in translational research and in the management of GCP compliant phase I-II and III clinical trials.

Selected publications:

Bertaina A, Zecca M, Buldini B, Sacchi N, Algeri M, Saglio F, Perotti C, Gallina AM, Bertaina V, Lanino E, Prete A, Barberi W, Tumino M, Favre C, Cesaro S, Del Bufalo F, Ripaldi M, Boghen S, Casazza G, Rabusin M, Balduzzi A, Fagioli F, Pagliara D, Locatelli F. Unrelated donor vs HLA-haploidentical/T-cell- and B-cell-depleted HSCT in children with acute leukemia. Blood. 2018 Dec 13;132(24):2594-2607.

Faraci M, Bertaina A, Luksch R, Calore E, Lanino E, Saglio F, Prete A, Menconi MC, De Simone G, Tintori V, Cesaro S, Santarone S, Orofino MG, Locatelli F, Zecca M. Sinusoidal obstruction syndrome/veno-occlusive disease after autologous or allogeneic hematopoietic stem cell transplantation in children: a retrospective study of the AIEOP-HSCT (Italian Hematology-Oncology Association-Hematopoietic Stem Cell transplantation) Group. Biol Blood Marrow Transplant. 2018 Sep 25. pii: S1083-8791(18)30594-9.

Messina C, Zecca M, Fagioli F, Rovelli A, Giardino S, Merli P, Porta F, Aricò M, Sieni E, Basso G, Ripaldi M, Favre C, Pillon M, Marzollo A, Rabusin M, Cesaro S, Algeri M, Caniglia M, Di Bartolomeo P, Ziino O, Saglio F, Prete A, Locatelli F. Outcomes of Children with Hemophagocytic Lymphohistiocytosis Given Allogeneic Hematopoietic Stem Cell Transplantation in Italy. Biol Blood Marrow Transplant. 2018 Jun;24(6):1223-1231.

Bruno B, Busca A, Vallero S, Raviolo S, Mordini N, Nassi L, Cignetti A, Audisio E, Festuccia M, Corsetti A, Depaoli L, Faraci M, Micalizzi C, Corcione S, Berger M, Saglio F, Caropreso P, Mengozzi G, Squadrone V, De Rosa FG, Giaccone L. Current use and potential role of procalcitonin in the diagnostic work up and follow up of febrile neutropenia in hematological patients. Expert Rev Hematol. 2017 Jun;10(6):543-550

Saglio F, Cena S, Berger M, Quarello P, Boccasavia V, Ferrando F, Pittana L, Bruno B, Fagioli F. Association between thymic function and allogeneic hematopoietic stem cell transplantation outcome: results of a pediatric study. Biol Blood Marrow Transplant. 2015 Jun;21(6):1099-105.

Saglio F, Hanley PJ, Bollard CM. The time is now: moving toward virus-specific T cells after allogeneic hematopoietic stem cell transplantation as the standard of care. Cytotherapy. 2014 Feb;16(2):149-59.

Saglio F, Berger M, Vassallo E, Nesi F, Gunetti M, Fazio L, Rustichelli D, Ferrero I, Fagioli F. Intrabone cord blood hematopoietic stem cell transplantation in a subset of very high-risk pediatric patients: a safety and feasibility pilot study. J Pediatr Hematol Oncol. 2012 Jul;34(5):359-63.

Cistaro A, Saglio F, Asaftei S, Fania P, Berger M, Fagioli F. The role of 18F-FDG PET/CT in pediatric lymph-node acute lymphoblastic leukemia involvement. Radiol Case Rep. 2015 Nov 6;6(4):503.

Muraro M, Mereuta OM, Saglio F, Carraro F, Cravero C, Fagioli F. Tumor-associated-antigens or osteosarcoma cell line lysates: two efficient methods for in vitro generation of CTLs with special regard to MHC-I restriction. Cell Immunol. 2011;266(2):123-9.

Berger M, Grignani G, Ferrari S, Biasin E, Brach del Prever A, Aliberti S, Saglio F, Aglietta M, Fagioli F. Phase 2 trial of two courses of cyclophosphamide and etoposide for relapsed high-risk osteosarcoma patients. Cancer. 2009 Jul 1;115(13):2980-7.

Berger M, Biasin E, Saglio F, Fagioli F. Innovative approaches to treatsteroid-resistant or steroid refractory GVHD. Bone Marrow Transplant. 2008 Oct;42 Suppl 2:S101-5.

Muraro M, Mereuta OM, Saglio F, Carraro F, Berger M, Madon E, Fagioli F. Interactions between osteosarcoma cell lines and dendritic cells immune function: An in vitro study. Cell Immunol. 2008 May-Jun;253(1-2):71-80.

Roberto Foà

Sapienza University, Rome, Italy

Roberto Foà is Professor of Hematology and Head of Hematology at the 'Sapienza' University of Rome. He earned his medical degree in Turin, Italy, and specialized in pediatrics and in hematology. He worked at the MRC Leukaemia Unit, Royal Postgraduate Medical School and Hammersmith Hospital of London between 1976 and 1979. He took a sabbatical at Memorial Sloan-Kettering Cancer Center, New York, between 1991 and 1992.

His main interests have been the biological characterization of acute and chronic lymphoproliferative disorders, the role of molecular biology in the diagnosis and monitoring of hematological malignancies, the role of

cytokines in lymphoid malignancies, gene profiling, microarray analyses and next generation sequencing in acute and chronic leukemias, as well as the design of innovative therapeutic strategies for hematological neoplasms.
Over the years, Professor Foà has received support from many national and international sources. He is part of the European Leukemia Network and referee for national and international funding agencies. He was chairman of the Scientific Committee of the 4th EHA (European Hematology Association) Congress, Barcelona in 1999, councilor of EHA until December 2002, and a member of the Education Committee of EHA until December 2005. Has been President of EHA (European Hematology Association) during the years 2009–2011. Has been chairman of the Education Committee and of the Outreach Unit of EHA up to June 2017.
He has been a member of the National Committee for Health Research for the Ministry of Health (Italy) until December 2010 He is chairman of the GIMEMA Working Party for chronic lymphoproliferative disorders, and member of the board of the Working Party for acute leukemias.
Professor Foà has authored, co-authored, and edited over 650 papers, reviews, and books. He has been co-editor of *Leukemia and Lymphoma*, and associate editor of the *British Journal of Hematology* and of *The Hematology Journal*. He has been editor-in-chief of *The Hematology Journal* up to December 2004 and of *Haematologica - The Hematology Journal* from January 2005 to February 2008.

Panayiotis Panayiotidis
National and Kapodistrian University of (NKUA) Athens, Greece

Graduated from the Medical School of University of Athens in 1982.
Trained in Haematology in the 1st Department of Internal Medicine, University of Athens (Head prof Faidon Fessas).
Diploma in Haematology 1992
Post graduate studies:

1984–1985	Karolinska Hospital, Stockholm, Hematology Clinic (Head Prof Peter Reisentaein).
1992–1996	Royal Free Hospital, London, Haematology Clinic (Head Prof. Victor Hoffbrand) as an ESMO fellow and Hon. Lecturer.

Present Position:

1996–present	National and Kapodistrian University of (NKUA) Athens, 1st Department of Propaedeutic Medicine, Laikon General Hospital, professor of Haematology. Head of the Haematology Research Laboratory, NKUA

Member of the ERIC and IG-CLL groups of ELN.
Member of the EUTOS commitee "path to cure group in CML" of the ELN
National representative for Greece in the EUTOS CML European Group of ELN.
Member of the Steering Committee of the EURO-SKI trial of ELN.
Member of Hellenic Society of Haematology (President 2017–2018)
President of the Educational committee of the Hellenic Society of Haematology (2018–2020)
158 publications in neoplastic hematologic diseases with >6000 citations

Antonio Cuneo
University of Ferrara

1988–1989	Visiting Scientist At Centre For Human Genetics; K.U.L. Leuven, Belgium During Studies For Ph.D. In Experimental Hematology, Then Frequent Short Stays Until 1995.
1990	Appointed as full-time Researcher at the Section of Hematology, University of Ferrara, with an established role in providing health care in the Hematology Unit of the Azienda Ospedaliero Universitaria in Ferrara
2001	Associate Professor of Hematology, University of Ferrara
2005	Full Professor of Hematology, University of Ferrara
2006	Director of Hematology Section – S. ANNA University Hospital, Ferrara
2011–2015	Coordinator Ph.D. Programme in Molecular Medicine and Pharmacology, University of Ferrara
2012–2017	Director of the Department of Specialistic Medicine at the University Hospital in Ferrara, Italy
February 2019	Full professor of Hematology University of Ferrara (50% Full Time Equivalent) and University of Parma (50% FTE

Università degli Studi - Via Ariosto, 35, 44121 Ferrara
Azienda Ospedaliero - Universitaria di Ferrara
Full Professor of Hematology University of Ferrara (50% full time equivalent)) and Parma (50% FTE)
Director of Hematology Section - Azienda Ospedaliero Universitaria Arcispedale S. Anna Ferrara
Scientific High School degree in 1978 with a final score of 60/60
July 16, 1984: Degree in Medicine with a final grade of 110/110 and honors
1990 "PhD" in Experimental Hematology, University of Modena
Teaching activity:
Hematology – Clinical Oncology – Laboratory Medicine –
Coordinator of teaching block: "Cell Growth" within the Ferrara-Maastricht Academic Medical Exchange program at the School of Medicine, University of Ferrara
Research activity:
Study of molecular cytogenetic lesions in hematopoietic neoplasms.
Scopus (2018): H index 43; citation index 5943
I participated as a member to the "project management" group, to the European study titled "Molecular Cytogenetic Diagnosis in Hematologic Malignancies" financed by Economic European Community (Project leader: Prof. A. Hagemeijer, Erasmus University, Rotterdam, The Netherlands). Project Biomed I Program, Concerted Action CT94-1703, years 1994–1997
Research projects holder
AIRC
MIUR PRIN
FIRB
"Ricerca Finalizzata" MOH
Expert in Clinical Trials conduction according to GCP

2001–2004	Member of the editorial board of *Leukemia*

Member of the editorial board of *Leukemia Research and Treatment*
Member of the advisory board of *Haematologica* for 5 years
Member of the Italian Society of Hematology and of Italian Society of Experimental Hematology

1997–2002	Member of Board of the Italian Society of Experimental Hematology
2007–2008	President of the Italian Society of Experimental Hematology for biennium
2006–2007	President of Interfaculty Specialist Degree Course of Medical-Pharmaceutical Biotechnologies for biennium
01/2011–12/2015	Coordinator of Ph.D. school of Pharmacology and Molecular Oncology
October 2015	President of the "College of the full professors of Hematology of the Italian universities"
August 2018	President of the Scientific Committee of the GIMEMA foundation

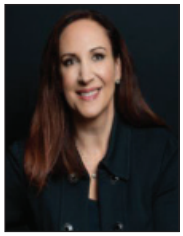
Robert Weinstein
Directors of the World Apheresis Association

Dr. Weinstein is a Phi Beta Kappa, Magna Cum Laude graduate of Brandeis University, Waltham, Massachusetts, where he majored in chemistry. After graduating from the New York University School of Medicine in New York City, he completed an internship and residency in Internal Medicine at the University of Miami Affiliated Hospitals program in Miami, Florida. He returned to New England as a fellow in hematology at the Beth Israel Hospital, Boston, where he stayed after completing his fellowship, as Assistant Professor of Medicine at Harvard Medical School. In 1985 he joined the Division of Hematology/Oncology at St. Elizabeth's Medical Center of Boston, a Tufts Medical School affiliate, where he established a program in therapeutic and donor apheresis. He later directed the Hematology and Transfusion Medicine section of the Division and became Professor of Medicine at Tufts. In 2006 he became the founding Chief of the Division of Transfusion Medicine at the UMass Memorial Medical Center, and University of Massachusetts Medical School, Worcester, Massachusetts, where he is Professor of Medicine, Pathology and Nursing and, among other duties, he is co-Director of the "Host Defense and Blood" course in the first-year medical school curriculum.
Dr. Weinstein has served as chair of the Hemapheresis Committee of AABB and chair of the Committee on Practice of the American Society of Hematology. He is past-president of the American Society for Apheresis, and of the World Apheresis Association. He served as Editor-in-Chief of the Journal of Clinical Apheresis from 2004 to 2015. He currently serves on the Board of Directors of the World Apheresis Association as Vice President for the Americas.

Joseph (Yossi) Schwartz
College of Physician, Surgeons of Columbia University

MD, MPH is a Professor of Pathology and Cell Biology at the College of Physician and Surgeons of Columbia University and the Director of the Transfusion Medicine & Cellular Therapy Service at the Columbia University Medical Center campus of the New York Presbyterian Hospital. As the Director of the Transfusion Medicine & Cellular Therapy Service, Dr. Schwartz oversees the Blood Bank, The Apheresis unit and the Cell Therapy facility. As a major tertiary & transplantation center, those facilities collect, receive & process blood products for transfusion in variety of indications such as patients with Sickle Cell Disease, complex cardiac surgery, Hematopoietic Progenitor Cell transplantation, and all types of solid organ transplantation. He was until recently the chair of the FACT-JACIE international standards for cellular therapy and he is currently the Immediate Past-President of the American Society for Apheresis (ASFA). He was part of the writing committee in the last 5 editions of ASFA's special issue published every 3 years describing current evidence-based clinical applications of Therapeutic Apheresis.

Jennifer Schneiderman
Ann & Robert H. Lurie Children's Hospital of Chicago



Education:

1993	B.S., General Health Science, Boston University
1994	M.S., Applied Physiology, Rosalind Franklin University of Medicine and Science/The Chicago Medical School
1998	M.D., Rosalind Franklin University of Medicine and Science/The Chicago Medical School
2006	M.S., Clinical Investigation, Northwestern University

Graduate medical education:

06/1998–06/2001	Pediatric Internship and Residency, Children's Hospital of Orange County, Orange, CA
07/2001–06/2002	Chief Resident, Children's Hospital of Orange County, Orange, CA
07/2002–06/2003	Pediatric Hematology Research Fellow, Children's Hospital of Orange County, Orange, CA
07/2003–06/2006	Pediatric Hematology/Oncology/Stem Cell Transplant Fellowship, Children's Memorial Hospital, Chicago, IL
07/2006–06/2007	Advanced Training in Stem Cell Transplantation Fellowship, Children's Memorial Hospital, Chicago, IL

Board certification and medical licensure:

10/2001–2018	General Pediatrics
11/2006–present	Pediatric Hematology/Oncology/Stem Cell Transplant
02/2000–07/2003	California Physician and Surgeon License
06/2003–present	Illinois Physician and Surgeon License

Academic appointments:

07/2006–07/2016	Assistant Professor of Pediatrics, Northwestern University, Feinberg School of Medicine, Chicago, IL
07/2016–present	Associate Professor of Pediatrics, Northwestern University, Feinberg School of Medicine, Chicago, IL

Hospital appointments:

2000–2003	Transport Team Physician, Children's Hospital of Orange County, Orange, CA
2001–2003	Attending Physician, Pediatrics, Children's Hospital of Orange County, Orange, CA
11/2010–present	Director, Therapeutic Apheresis Center, Lurie Children's Hospital, Chicago, IL
11/2017–present	Director, Pediatric Heme/Onc/Neuro-Onc/Stem Cell Fellowship program, Lurie Children's Hospital, Chicago, IL

Honors and awards:

2010–2016	Annual recipient, "Faculty Excellence in Education Award"
2010–2016	Annually recognized by graduating senior resident class with invitation to Chairman's Dinner
2010–2011	Recipient, Robert J Winter, M.D. Outstanding Teacher of the Year Award

Professional organizations:
American Society for Blood and Marrow Transplantation (ASBMT), member
Pediatric Blood and Marrow Transplant Consortium Registry Committee (03/2010–04/2014)
Pediatric Blood and Marrow Transplant Consortium Data and Safety Monitoring Committee (08/2012–present)
American Society for Apheresis (ASFA), member
Inaugural Member, ASFA Pediatric Subcommittee (08/2010–present)
ASFA Rare Disease Subcommittee (03/2012–2016)
Inaugural Chair, ASFA Extracorporeal Photopheresis Subcommittee (06/2013–05/2019)
ASFA Organizing Committee for the 2018 annual meeting
Invited member, JCA Special Issue Committee, submitted for publication 05/2019
Co-chair, Clinical Applications Committee (09/2018–05/2019)
Chair, Clinical Applications Committee (05/2019–present)
Elected to ASFA Board of Directors (05/2019–present)
Chair, Organizing Committee, ASFA 2019 State of the Science Conference on Extracorporeal Photopheresis, (05/2019)
American Council on ECP (ACE), Co-founder, April 2017
Planned and facilitated our first scientific meeting along with the other two co-founders, Drs. Edelson and Wu
American Society of Hematology, member
American Society of Transplantation, member
Professional activities:
Institutional Service:

1998–2003	Curriculum Committee, Children's Hospital of Orange County, Orange, CA

2001–2003	Evaluation Committee, Children's Hospital of Orange County, Orange, CA
2001–2003	GMEC Committee, Children's Hospital of Orange County, Orange, CA
10/2008–present	Stem Cell Transplant Quality and Safety Committee, Northwestern University
04/2011–2017	Scientific Review Committee, Lurie Cancer Center, Northwestern University
01/2014–present	Family Centered Work Rounds Organizational Committee, Northwestern University
11/2017–present	Fellowship director, Pediatric Hematology/Oncology/ Neuro-Oncology/Stem Cell Transplantation, Northwestern University

Teaching:

1994–1995	Teaching Assistant, Histology, Chicago Medical School
1994–1995	Teaching Assistant, Physiology, Chicago Medical School
2012–present	General stem cell transplant lectures to PICU and ID fellows; approximately 2 hours per year
2007–present	General stem cell transplant lectures to rotating house staff; 12 - 14 hours per year
2012–present	"Apheresis Pearls" lecture to Heme/Onc/SCT fellows; approximately 2 hours per year

Trainees:

09/2014–present	Inaugural member, Clinical Competency Committee, Heme/Onc/Stem Cell Transplant fellowship program, Northwestern University
2014–2016	Member, Scholarly Oversight Committee for pulmonary fellow Matthew Abts, MD

Extramural Membership/Advocacy:

05/2008–present	Board of Directors, Children's Oncology Services, Inc.
05/2008–present	Medical Committee, Children's Oncology Services, Inc.
10/2013–10/2014	Executive Committee, Children's Oncology Services,
05/2015–present	Inc.
03/2015–present	Programs Compliance Working Group, Children's Oncology Services, Inc.
01/2012–06/2014	Board of Directors, Recovery on Water
04/2012–11/2014	Data Safety Monitoring Board for United Therapeutics Corporation's trial: "A Comparative Pharmacokinetic and Safety Study of Chimeric Monoclonal Antibody CH14.18 with Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF), Interleukin-2 (IL-2), and Isotretinoin in High Risk Neuroblastoma Patients Following Myeloablative Therapy"

Editorial Responsibilities:

07/2015–present	Associate Editor, *Journal of Clinical Apheresis*

Reviewer Responsibilities:

Ad hoc reviewer for Journal of Clinical Apheresis, Journal of Pediatric Hematology/Oncology, and Vox Sanguinis

Grant awards:

Named "Hyundai Scholar" for 2008, awarded $50,000 for "Reduced Intensity Stem Cell Transplant in Children and Young Adults Utilizing Photopheresis, Fludarabine, and Busulfan."

Division of Heme/Onc/Stem Cell Transplant Seed Grant, "Extracorporeal Photopheresis (ECP) in Combination with Drug Based Immunosuppressive Agents in the Prevention of Cardiac Allograft Rejection in a Small Animal Model," awarded $21,000, 01/2014

Co-PI, grant from Transimmune, "Role of parallel-plate flow chambers in ECP induced cardiac transplant tolerance in mice," awarded $40,000, 09/2014.

Northwestern University 2016 Dixon Translational Research Grant, "Extracorporeal Photopheresis (ECP) as a Novel Strategy for Transplant Tolerance Induction," awarded $50,000, 11/2015

Northwestern University 2017 Stanley Manne Visionary Award, "Safety and Efficacy of ECP Treated Donor Cells in Prevention of Allograft Rejection and Xenogenic GVHD," awarded 08/2017.

Invited lectures:

10/2006	"Extracorporeal Photopheresis in Children Following Hematopoietic Stem Cell Transplant – The Children's Memorial Experience." Symposium, "Exracorporeal Photo-immunotherapy in Pediatric Patients," Essen, Germany,; sponsored by Therakos, Inc.
09/2007	Chicago's Pediatric Cancer Care Coalition Educational Symposium: "Living Beyond Childhood Cancer: Stem Cell Transplantation,"
02/2009	"The use of Extracorporeal Photopheresis in the Pediatric Patient," ASFA Webinar,
05/2009	"Extracorporeal Photopheresis in Pediatric Stem Cell Transplantation," ASFA annual meeting,
05/2010	"Challenges in Pediatric Apheresis," ASFA annual meeting,
06/2011	"Pediatric ECP," ASFA annual meeting,
10/2016	"The Use of Extracorporeal Photopheresis in GVHD," AABB annual meeting "RAP Session,"
05/2017	"Inducing HLA-Mismatched Allograft Survival with ECP Treated Donor Leukocytes," ASFA annual meeting, Opening Scientific Symposium,
10/2017	"ECP: Cellular Therapy for the Treatment of Acute and Chronic Graft-versus-Host Disease," AABB annual meeting,
12/2017	"ECP: Cellular Therapy for the Treatment of Acute and Chronic Graft-versus-Host Disease," Educational Session at the ASH annual meeting,
04/2018	"ECP for the Treatment of Acute and Chronic Graft-versus-Host Disease," ASFA annual meeting,
05/2019	"Innovative Approach to Antigen Specific Tolerance Induction: Entering the Scientifically Driven Phase of ECP," ASFA 2019 State of the Science Conference on Extracorporeal Photopheresis,

Publications:

Original Investigations:

Schneiderman J, Nugent DJ, Young, G. Sequential therapy with activated prothrombin complex concentrate and recombinant factor VIIa in patients with severe haemophilia and inhibitors. *Haemophilia* 2004; 10:347-51.

Schneiderman J, Rubin E, Nugent DJ, Young, G. Sequential therapy with activated prothrombin complex concentrate and recombinant factor VIIa in patients with severe haemophilia and inhibitors: update of our previous experience. *Haemophilia* 2007 May; 13(3):244-8.

Schneiderman J, London WB, Brodeur GM, Castleberry RP, Look AT, Cohn S. Clinical Significance of MYCN Amplification and Ploidy in "Favorable" Stage Neuroblastoma: A Report from the Children's Oncology Group. *Journal of Clinical Oncology* 2008;26(6):913-918.

Schneiderman J. Non-pharmacologic strategies in hematopoietic stem cell transplantation. *Current Pharmaceutical Design*. 2008;14(20):1987-96.

Tse WT, Duerst R, Schneiderman J, Chaudhury S, Jacobsohn DA, Kletzel M. Age-dependent pharmacokinetic profile of single daily dose IV busulfan in children undergoing reduced-intensity conditioning stem cell transplant. *Bone Marrow Transplantation.* 2009 August;44(3):145-56.

Schneiderman J, Jacobsohn DA, Collins J, Thormann K, Kletzel M. The Use of Fluid Boluses to Safely Perform Extracorporeal Photopheresis (ECP) in Low-weight Children: A Novel Procedure. *Journal of Clinical Apheresis*. 2010;25(2):63-9.

Andolina JR, Kletzel M, Tse WT, Jacobsohn DA, Duerst RE, Schneiderman J, Helenowski IB, Rademaker A, Chaudhury S. Allogeneic hematopoietic stem cell transplantation in pediatric myelodysplastic syndromes: improved outcomes for de novo disease. *Pediatric Transplantation.* 2011 May;15(3):334-43.

Martin A, Schneiderman J, Helenowski IB, Morgan E, Dilley K, Danner-Koptik K, Hatahet M, Shimada H, Cohn SL, Kletzel M, Hijiya N. Secondary Malignant Neoplasms after High-Dose Chemotherapy and Autologous Stem Cell Rescue for High-Risk Neuroblastoma. *Pediatric Blood and Cancer*. 2014 Aug;61(8):1350-6.

Delaney M, Capocelli KE, Eder AF, Schneiderman J, Schwartz J, Sloan SR, Wong EC, Kim HC. An International Survey of Pediatric Apheresis Practice. *Journal of Clinical Apheresis*. 2014 April;29(2):120-6.

Ratcliffe N, Dunbar NM, Adamski J, Couriel D, Edelson R, Kitko CL, Levine JE, Morgan S, Schneiderman J, Sloan S, Wu Y, Szczepiorkowski ZM, Cooling L. National Institutes of Health State of the Science Symposium in Therapeutic Apheresis: Scientific Opportunities in Extracorporeal Photopheresis. *Transfusion Medicine Reviews*. 2015 Jan;29(1):62-70.

Ward J, Kletzel M, Duerst R, Fuleihan R, Chaudhury C, Schneiderman J, Tse W. Single Daily Busulfan Dosing for Infants with Non-Malignant Diseases Undergoing Reduced Intensity Conditioning for Allogeneic Hematopoietic Progenitor Cell Transplantation. *Biology of Blood and Marrow Transplantation*. 2015 Sept;21(9):1612-21.

Pham HP, Schwartz J, Cooling L, Hofmann JC, Kim H, Morgan S, Pagano MB, Schneiderman J, Winters JL, Yamada C, Wong EC, Wu Y. Report of the ASFA Apheresis Registry Study on Wilson's Disease. *Journal of Clinical Apheresis*. 2016 Feb;31(1):11-15.

Curi DA, Duerst RE, Badke C, Bell J, Chaudhury S, Kletzel M, Schneiderman J, Tse WT, Muller WJ, Hijiya N. Intravenous Pentamidine for Pneumocystis jiroveci Pneumonia Prophylaxis in Pediatric Allogeneic Stem Cell Transplant Patients. *Bone Marrow Transplantation*. 2016 Oct;51(10):1394-1396.

Broglie L, Hijiya N, Helenowski IB, Dilley K, Schneiderman J, Tse WT, Duerst RE, Kletzel M, Morgan E, Chaudhury C. Long Term Follow-up of Children with Chronic Myeloid Leukemia After Hematopoietic Stem Cell Transplantation and Tyrosine Kinase Inhibitor Therapy. *Leukemia Lymphoma*. 2016;57(4):949-52.

Dunbar NM, Raval JS, Johnson A, Abikoff CM, Adamski J, Cooling LL, Grossman B, Kim HC, Marques MB, Morgan S, Schmidt AE, Sloan SR, Su LL, Szczepiorkowski ZM, West FB, Wong E, Schneiderman J. Extracorporeal Photopheresis Practice Patterns: An International Survey by the ASFA ECP Subcommittee. *Journal of Clinical Apheresis*. 2017 Aug;32(4):215-223.

Armstrong AE, Smyth E, Helenowski IB, Tse WT, Duerst RE, Schneiderman J, Kletzel M, Chaudhury S. The Impact of High-Resolution HLA-A, HLA-B, HLA-C, and HLA-DRB1 on Transplant-related Outcomes in Single-unit Umbilical Cord Blood Transplantation in Pediatric Patients. *Journal of Pediatric Hematology/Oncology*. 2017 Jan;39(1):26-32.

Broglie L, Helenowski IB, Jennings L, Schafernak K, Duerst R, Schneiderman J, Tse WT, Kletzel M, Chaudhury S. Early Mixed T-cell Chimerism is predictive of Pediatric AML or MDS Relapse after Hematopoietic Stem Cell Transplant. *Pediatric Blood and Cancer*. 2017 Sep;64(9).

DeSimone R, Schwartz J, Schneiderman J. "Extracorporeal Photopheresis in Pediatric Patients: Practical and Technical Considerations." *Journal of Clinical Apheresis*. 2017 Dec;32(6):543-552.

Armstrong AE, Danner-Koptik K, Golden S, Schneiderman J, Kletzel M, Reichek J, Gosiengfiao Y. Late Effects in Pediatric High-risk Neuroblastoma Survivors After Intensive Induction Chemotherapy Followed by Myeloablative Consolidation Chemotherapy and Triple Autologous Stem Cell Transplants. Journal of Pediatric Hematology and Oncology. 2018 Jan;40(1):31-35.

Schneiderman J. "Extracorporeal photopheresis: cellular therapy for the treatment of acute and chronic graft-versus-host disease." *Hematology 2017* (Am Soc Hematol Educ Program) Dec 8;2017(1):639-644.

Broglie L, Rademaker A, Galvin J, Ray A, Tse WT, Duerst RE, Schneiderman J, Kletzel M, Chaudhury S. "Fecal Calprotectin and Serum Albumin as Markers of Gastrointestinal Graft-Versus-Host Disease." *Hematology/Oncology and Stem Cell Therapy*. 2018 Sept;11(3):169-174.

Edelson R, Wu Y, Schneiderman J. "American Council on ECP (ACE): Why now?" *Journal for Clinical Apheresis.* 2018 Aug;33(4):464-468.

Rossoff JE, Tse WT, Duerst RE, Schneiderman J, Morgan E, Kletzel M, Chaudhury S. High-dose chemotherapy and autologous hematopoietic stem cell rescue for treatment of relapsed and refractory Wilms tumor: Re-evaluating outcomes. *Pediatric Hematology and Oncology*. 2018 Aug – Sep;35(5-6):316-321.

Reviews & Case Reports:

Schneiderman J, Thormann K, Charrow J, Kletzel M. Correction of Enzyme Levels with Allogeneic Hematopoeitic Progenitor Cell Transplantation in Niemann-Pick Type B. *Pediatric Blood and Cancer* 2007 December; 49(7):987-9.

Schneiderman J. Non-Pharmacologic Strategies in Hematopoietic Stem Cell Transplantation. *Current Pharmaceutical Design*. 2008;14(20)1987-96.

Schneiderman J. Management and Prevention of Graft-Versus-Host Disease Following Hematopoietic Stem Cell Transplantation in Pediatric Patients with Extracorporeal Photopheresis. *The Asia-Pacific Journal of Oncology & Hematology*.

Walz A, Lenzen A, Curtis B, Canner J, Schneiderman J. Use of Allogeneic Stem Cell Transplantation for Moderate-Severe Glanzmann Thrombasthenia. *Platelets*. 2014 Dec 30:1-3.

Badaway SM, Becktell K, Muller WJ, Schneiderman J. *Aspergillus* Thyroiditis: First Antemortem Case Diagnosed by FNA Culture in a Pediatric Stem Cell Patient. *Transplantation Infectious Diseases*. 2015 Dec; 17(6):868-71.

Rossoff JE, Schneiderman J, Chaudhury S, Arva NC. Diagnostic utility of Complement immunohistochemical studies in post-stem cell transplant intestinal thrombotic microangiopathy: Case report. *Journal of Pediatric Hematology and Oncology*. 2017 May;39(4):282-286.

Book Chapter:

Schneiderman J and Walterhouse DO. Hematologic and Oncologic Emergencies. *Pediatric Hospital Medicine*, 2nd Edition, 2007, pp 352-358, Lippincott Williams & Wilkins.

Abstracts:

"Sequential Therapy with Activated Prothrombin Complex Concentrate and Recombinant Factor VIIa in Patients with Severe Hemophilia and Inhibitors," American Society of Hematology Annual Meeting, 12/2003

"Niemann-Pick Type B: Successful Allogeneic Hematopoeitic Stem Cell Transplantation with Correction of Enzyme Levels," American Society for Blood and Marrow Transplantation Annual Meeting, 02/2005

"Arteriovenous Fistula with Aneurysmal Dilitation: An Unusual Complication of Sickle Cell Disease and Moya Moya," National Sickle Cell Disease Program Annual Meeting, 4/05

"Tandem High Dose Therapy with Hematopoietic Progenitor Cell Rescue in Children with High-Risk Solid Tumors," American Society for Blood and Marrow Transplantation Annual Meeting, 02/2006

"Sequential rFVIIa and FEIBA for the Management of Bleeding Episodes in Inhibitor Patients: Update from our Previous Report," World Federation of Hemophilia Annual Meeting, 05/2006

"Hyperdiploidy is Associated with Favorable Outcome in Patients with MYCN-amplified POG Stage A, B, and Ds Neuroblastoma," Advances in Neuroblastoma Research Annual Meeting, 05/2006

"Reduced Intensity Conditioning and Hematopoietic Stem Cell Transplantation Utilizing Extracorporeal Photopheresis, Fludarabine, and Targeted Single Dose Busulfan as an Outpatient Procedure in Children. Preliminary Results," American Society for Blood and Marrow Transplantation Annual Meeting, 02/2007

"Donor Chimerism Kinetics in Pediatric Patients Undergoing Reduced Intensity Conditioning (RIC) with Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)," American Society for Blood and Marrow Transplantation Annual Meeting, 02/2008

"Use of Stem Cell Transplantation for Moderate-Severe Glanzmann Thrombasthenia," American Society of Pediatric Hematology/Oncology Annual Meeting, 04/2013

"Pharmacokinetics (PK) using a test dose to calculate a therapeutic single daily dose of I.V. Busulfan (BU) as part of reduced intensity conditioning (RIC) for allogeneic hematopoietic stem cell transplantation (HSCT) in infants less than 1 year of age," Primary Immune Deficiency Treatment Consortium (PIDTC) Annual Workshop, 05/2013

"Neck Tenderness as an Initial Presentation of Disseminated Aspergillosis: Is Fine Needle Aspiration an Option or a Must?" American Society for Blood and Marrow Transplantation Annual Meeting, 02/2014

"An International Survey of Pediatric Apheresis Practice," American Society for Apheresis, *oral presentation* 04/2014 (contributing author)

"Report of the ASFA Apheresis Registry," American Society for Apheresis, oral presentation, 04/2014 (contributing author)

"Report of the ASFA Apheresis Registry Study on Wilson's Disease," American Society for Apheresis, *oral presentation*, 04/2014 (contributing author)

"Chronic Graft-versus-host Disease of the CNS: A Rare Autopsied Case," American Society for Blood and Marrow Transplantation Annual Meeting, 02/2015
"Single Infusion of Donor-Type Splenocytes with Extracorporeal Photopheresis Prior to Transplantation Significantly Prolongs Cardiac Allograft Survival in Mice." American Transplant Congress annual meeting, 05/2015 (first author)
"Pre-Transplant Infusion of Extracorporeal Photopheresis Treated Donor Splenocytes Leads to Long-Term Liver Allograft Survival and Donor Specific Tolerance in Rats." American Transplant Congress annual meeting, *oral presentation*, 05/2016 (co-senior author)
"Extracorporeal Photopheresis Practice Patterns: An International Survey by the ASFA ECP Subcommittee." American Society for Apheresis, *oral presentation*, 05/2016 (senior author)

Anand Padmanabhan
Medical College of Wisconsin

Dr. Padmanabhan is a member of the Medical Sciences Institute and Blood Research Institute at Versiti Wisconsin and Associate Professor at the Medical College of Wisconsin. He received his medical degree (MBBS) from Thanjavur Medical College, India, Masters and PhD from Brown University (Providence, RI, USA) and underwent residency and fellowship training at the College of Physicians and Surgeons of Columbia University (New York, NY, USA) and the Institute for Transfusion Medicine (Pittsburgh, PA, USA), respectively. He serves as Medical Director for Cellular Collection (Apheresis) of the Blood and Marrow Transplant and Effector Cell Therapy programs at the Medical College of Wisconsin. In addition to expertise and interest in the area of cellular collections, his clinical interests include facilitation of immunologically challenging renal transplants. Dr. Padmanabhan also directs an NIH-funded laboratory focused on understanding the pathophysiology of Heparin-induced thrombocytopenia (HIT), a dangerous thrombotic disorder. The emphasis of his HIT research is on developing better ways to diagnose and treat this condition.

Angelo Maiolino
Professor of Medicine, Department of Internal Medicine, Universidade Federal do Rio de Janeiro (UFRJ)

Coordinator of Hematology, Americas Centro de Oncologia Integrado, Rio de Janeiro, Brazil
Graduate in Medicine (1982), Universidade Federal do Estado do Rio de Janeiro
Residence in Internal Medicine and Hematology (1986–88) at the University Hospital Clementino Fraga Filho, Federal University of Rio de Janeiro.
Fellow in Hematology and Bone Marrow Transplantation at the Hospital San Martino, Genova, Italy (1986–1988)
PhD in Internal Medicine - Hematology, Federal University of Rio de Janeiro (2000)
Professor of Medicine, Department of Internal Medicine, Federal University of Rio de Janeiro.
Chief of Hematology Service, Americas Centro de Oncologia Integrado, Rio de Janeiro
Member of the "International Myeloma Working Group"

Evangelos Terpos
Clinical Therapeutics of the National & Kapodistrian University of Athens

MD, PhD is a Professor of Hematology in the Department of Clinical Therapeutics of the National & Kapodistrian University of Athens, School of Medicine, Athens, Greece.
His main research interest is the biology of plasma cell dyscrasias and especially the biology of bone disease in multiple myeloma (MM). Dr Terpos has reported the significant role of RANKL and osteoprotegerin axis, CCL-3 (MIP-1a), Wnt and TGF-beta signaling in myeloma bone disease and myeloma cell growth. He has studied the predictive value of markers of bone remodeling and osteoclast function in myeloma progression and patients' survival. He has evaluated the effect of bisphosphonates and different anti-myeloma therapies including ASCT, IMiDs- and bortezomib-based regimens on bone metabolism. He has studied the biology and prevalence of osteonecrosis of the jaw in myeloma patients who receive bisphosphonates. Dr Terpos also works on the role of modern imaging (including whole-body low-dose CT and MRI) for MM, of angiogenesis in MM and Waldenstrom's Macroglobulinemia, and of renal impairment in MM. In the clinical research era, Dr Terpos participates in several important clinical trials with novel agents (pomalidomide, carfilzomib, ixazomib, daratumumab, elotuzumab, isatuximab, anti-BCMA, etc) in the field of multiple myeloma. Dr Terpos is also interested in the biology and management of bone disease in other hematology disorders, including hemoglobinopathies, hemophilia and histiocytosis. This research work was reported in more than 500 papers in peer-reviewed journals and Dr Terpos has 17,650 citations and an h-index of 68 in ISI/Web of Knowledge (August 2019).
Dr Terpos is co-chairing the Bone Subgroup of the International Myeloma Working Group and the Guideline Subgroup of the European Myeloma Network. He was member of the Board of the Greek Society of Hematology (2015-2016) and Vice-President of this Society for 2017-2018. Dr Terpos has given lectures at ASH, ASCO & EHA meetings, International Myeloma Workshops, International Meetings on Cancer-Induced Bone Disease and in several national meetings. He is reviewer of scientific papers in more than 50 medical journals and has reviewed abstracts for ASH, EHA & EBMT meetings. He is Associate Editor of *HemaSphere* (official journal of EHA) for Myeloma.

Albert Donnenberg
The University of Pittsburgh School of Medicine

Studied Philosophy as an undergraduate at the University of Colorado, Boulder. He received his Ph.D. in Infectious Disease Epidemiology at the Johns Hopkins University in 1980, studying cellular immunity to Herpes Simplex Virus. Upon graduation he was elected to Delta Omega, the honorary Public Health Society. After a postdoctoral fellowship under the direction of Dr. George Santos at the Johns Hopkins Oncology Center, Dr. Donnenberg was appointed Instructor of Oncology in 1982, Assistant Professor in 1983, and Associate Professor in 1989. He worked on adoptive transfer of donor immunity during allogeneic bone marrow transplantation, and on the development and clinical implementation of T-cell depletion of bone marrow to prevent graft versus host disease. He also performed early studies on cellular immunity in HIV infection, and co-developed the concept of T-cell homeostasis. In 1991, Dr. Donnenberg was recruited to the University of Pittsburgh to serve as the Director of Laboratory Research in the Bone Marrow Transplant Program. He has also served as program Co-director, and as Interim Director. He has directed the UPMC Adult Hematopoietic Stem Cell Laboratory and since 1998 and the UPMC Pediatric Hematopoietic Stem Cell Laboratory and since 2000 and serves as a team leader and flow cytometry inspector for the American College of Pathology. He was promoted to Professor of Medicine in 2001. From 1998 to 2018 he also directed the University of Pittsburgh Cancer Center's Cytometry Facility. He currently holds appointments at The University of

Pittsburgh School of Medicine as a Professor of Medicine with tenure, the University of Pittsburgh Graduate School of Public Health as Professor of Infectious Diseases and Microbiology and is a member of the McGowan Institute of Regenerative Medicine. His current research interests are in cellular therapy and graft engineering, the role of stem cells in neoplasia, and immunotherapy for metastatic cancer, projects he pursues with his scientific and life partner Dr. Vera Donnenberg. He is an internationally recognized expert in therapeutic cell processing and flow cytometry. Dr. Donnenberg has co-edited two editions of the CRC Handbook of Human Immunology and has authored more than 200 scholarly publications. He is the proud father of 4 daughters and one son and the grandfather of a boy and a girl. He and Vera live on Pittsburgh's Southside where their hobbies are winemaking and collecting art.

Vera S. Donnenberg
University of Pittsburgh, Pittsburgh, Pennsylvania

Ph.D., FCP, a Regent of the Board of the American College of Clinical Pharmacology, is currently Associate Professor, Department of Cardiothoracic Surgery, School of Medicine and Department of Pharmaceutical Sciences, School of Pharmacy, University of Pittsburgh, Pittsburgh Pennsylvania, where she leads a group of basic cancer scientists, students and research fellows focused on basic and translational cancer research. She is also a delegate to the Association of American Medical Colleges (AAMC) and an Administrative Board member of the AAMC Council of Faculty and Academic Societies.
In the University of Pittsburgh School of Medicine, she serves as the Director of Basic Research, The Heart, Lung and Esophageal Surgery Institute and is the Vice Chair for Academic Advancement for the Department of Cardiothoracic Surgery, where she advises and manages faculty promotions. Vera received her M.S. in Clinical Pharmacology from The Johns Hopkins University earned her Ph.D. in Pharmaceutical Sciences from the University of Pittsburgh, School of Pharmacy. She is an Era of Hope Scholar for the Department of Defense Congressionally Directed Medical Research Programs. She also serves on multiple committees of various international academic societies, serves as a reviewer for national and international peer reviewed grant awards and foundations and is a permanent member of several study sections. Vera is also an adjunct faculty consultant at the Carnegie Mellon University School of Drama, Graduate Dramatic Writing Program, lecturing on the role of science in fiction (although at times it seems that it should be the other way around). Vera has received over 30 national and international awards for her academic and service efforts including the Marylou Ingram Woman in Science Award from the Coulter Foundation, the Governor's Distinguished Citizenship Award, Maryland, and the Service Award from the National Society of Black Engineer. She is a member of several editorial boards and is and Associate Editor of *Cytometry, Stem Cells*, a leading journal in the field of imaging and cytometry. Vera's research interests have focus on therapeutic resistance in cancer, transplantation and HIV.

Khalid Halahleh
Internal Medicine King Hussein Cancer Center

Consultant, medical oncologist with good hematology and stem cell transplantation experience. Highly motivated, team-oriented Jordanian and Palestinian Board Certified in Internal Medicine and Medical Oncology Physician with more than 10 year experience in the field of malignant hematology oncology with experience in treating patients with leukemia, Lymphoma, myeloma and stem cell transplantation. I joined King Hussein Cancer Center, as a consultant of Medical Oncology and bone marrow transplantation in the department of internal medicine starting 21th of February, 2016 and I am holding my post till present time. I graduated from Rostove on Done Medical university in Russia in 1999, had my internship in Makassed Islamic charitable Hospital in 2000 and Internal Medicine residency Program at AVH hospital in Jerusalem in 2003. I did my medical oncology fellowship at King Hussein Cancer Center between 2003–2006 I had my training in bone marrow transplantation in Hadassah Hospital in Jerusalem in 2008–2009.
I worked at AVH CCC in Jerusalem as consultant Medical Oncology between 2007–2013 and I established first hematology service in Palestine, treating malignant hematology patients and I established the first bone marrow transplantation unit for high dose chemotherapy and autologous stem cell transplantation there. Between 2013–2016, I joined Sheba Medical center in Tel-Hashomer as a staff physician working in hematology and bone marrow transplant section. In February 2016, I joint King Hussein Cancer Center as consultant of Medical Oncologist and Bone marrow transplantation and cell therapy and I am holding my post till present time.
My interest is treating malignant hematology patients including acute leukemias and MDS from induction chemotherapy to an allogeneic stem cell transplantation, haploidentical transplant program at KHCC. My research activities include study the use of prophylactic HMA in AML and MDS after allogeneic Hematopoietic Stem cell Transplantation, I am co-investigator on a phase III randomized open-label multi-center study of Roxolitinib vs best available therapy in patients with corticosteroid-refractory chronic graft versus host disease after allogeneic stem cell transplantation (REACH-3) and Investigating the impact of infused Hematopoietic stem cell subsets on graft failure in Non-Malignant disorders, Intramural grant application.
I had several publications, most recent one in the BMT journal May 2019, titled Hematopoietic cell transplants in Jordan: different indications from the US and EU.

Nathaniel S. Treister
Brigham and Women's Hospital, Boston, USA and Harvard School of Dental Medicine, Boston, USA

Dr. Treister is Chief of the Divisions of Oral Medicine and Dentistry at Brigham and Women's Hospital and Dana-Farber Cancer Institute in Boston, Massachusetts. Dr. Treister earned his DMD from the University of Pennsylvania School of Dental Medicine and subsequently completed his Oral Medicine certificate and Oral Biology doctoral training at the Harvard School of Dental Medicine, where he is an Associate Professor of Oral Medicine in the Department f Oral Medicine, Infection and Immunity. He is board certified in Oral Medicine and practices at Brigham and Women's Hospital, Dana-Farber Cancer Institute, and Boston Children's Hospital with special interest in oral mucosal diseases, salivary gland diseases, and oral complications in cancer patients. He has published extensively in the field of oral medicine with an emphasis on oral complications of stem cell transplantation and oral graft-versus-host disease.

Prasad S. Adusumilli
Memorial Sloan-Kettering Cancer Center, New York

My research focuses on tumor immunology, chimeric antigen receptor (CAR) T-cell therapy, and combination immunotherapy for solid tumors. Over the years, our research has yielded mechanistic data that has been translated to CAR T-cell and combination immunotherapy clinical trials for patients with lung cancer, mesothelioma, and breast cancer. Our laboratory research has been funded by >70 grant awards resulting in >200 publications. In addition to serving on medical journal editorial boards, I am the Deputy Editor for *Molecular Therapy Oncolytics.*

Jean-François Rossi
University of Montpellier

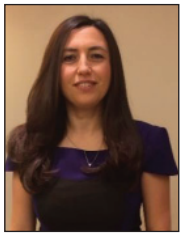
He is professor of Hematology at the University of Montpellier. He has over 30 years of experience in medicine and was certified in Rhumatology, Medical Oncology, Hematology, Immunology and Internal Medicine. He received his MD and PhD degrees in Hematology Immunology at the University of Montpellier and had post-doc at the Universities of Arizona (Tucson) and San Antonio (Texas) for multiple myeloma and bone research. He was associate professor at the University of Suzhou (China) for more than 10 years. He is member of 7 international scientific societies and the Scientific Advisory Board of the Castleman Disease Collaborative Network (CDCN). He was in charge of Medical Oncology for 5 years in Montpellier Cancer Center. He became the head of the Hematology Department during 14 years and he developed with Professor Bernard Klein the Biotherapy Saint-Eloi site (Immunotherapy-Regenerative Medicine (Chu/Inserm/University). He is particularly active in Immunotherapy for cancer and programs on crossed information analysis for algorithms including epigenetics with microbiota with 198 PubMed publications and 4 patents. He participated or activated different clinical or bio-clinical research programs with pharmaceutical companies (more than 150) or with academic institutes. He obtained an Award from the American Association for Cancer Research on April 2017 for his work on inflammatory process and interleukin 6 (http://aacrjournals.org/content/j-f-rossi-bio and The Best of the AACR Journals).

He was a consultant for different for more than 20 years, in the domain of immune precision medicine and the development of different drugs, notably siltuximax (Centocor, EUSAPHARMA) TACI-Ig (Serono Merck), IPH1101 (Innate Pharma), anti-CD20 LFB-R603 (LFB), polyoxidinium (Petrovax Pharm LLC), POC for Horiba Medical, and for Marc Cluzel, Sanofi Research. He participated to the creation of 4 start-ups. He is an active member of the Scientific Advisory Boards for 3 start-ups such as Urodelia and Beta Innov.

With E-Sana as a co-founder with Pr Kalle Levon (Polytechnic Institute of NYU, Brooklyn, USA) and Césare Massart, he participates to new programs based on innovative technology for tests including in-Home and biological monitoring, with dynamic follow-up.

Nowadays, he develops a new Institute For Precision Medicine and Immunotherapy at the Cancer Institute Sainte Catherine, Avignon, France, with the collaboration of LABOSUD/INOVIE, academic labs (linked to the University Hospital in Montpellier and the Institute Paoli-Calmette, in Marseille) and start-ups. This platform integrates an international scientific committee and will use new technologies in Telemedicine.

Özlem Er
Acıbadem University Medical Faculty, İstanbul, Turkey



Professor Er is a Professor of Internal Medicine and Medical Oncology and Head of Department of Medical Oncology at Acıbadem University Medical Faculty, İstanbul, Turkey. Professor Er is the board member of Turkish Medical Oncology Society.

Professor Er graduated from Hacettepe University Medical School in 1994. She became Internal Medicine Specialist in 1999 and a Medical Oncology Specialist in 2002. She was a clinical observer under supervision of Prof Gabriel N. Hortobagyi in the Medical Oncology Department at MD Anderson Cancer Center, and an AVON-AACR Cancer Biology Fellow at Thomas Jefferson University, Philadelphia, PA As one of the 8 researchers worldwide who won the AVON project award – Association for American Cancer Researches (AACR) in 2006-2008, she stayed at Thomas Jefferson University performing experimental studies on breast cancer. She contributed to significant studies on cancer stem cells and cancer development. She also received numerous awards including 29th ESMO Travel Award (Vienna, 2004), Journal of Thrombosis and Haemostasis 2004 Young Investigator Prize and Avon Foundation-American Association for Cancer Research International Scholars Award in Breast Cancer Research (2006).

Professor Er published in multiple international and national journals in the field of oncology, particularly breast, lung, gastric, colorectal (intestinal) cancers.

Sernaz Uzunoğlu
Trakya University Hospital, Edirne, Turkey

Education:

1981–1987	Private Işık High School
1987–1993	Istanbul University, Cerrahpaşa Medical Faculty
1993–1998	Residency period in Istanbul University, Cerrahpaşa, Faculty of Medicine, Department of Internal Medicine
1998–2005	İnternal Medicine Specialist in Haseki Education and Research Hospital, 3rd internal clinic
2006–2009	Residency period in Trakya University Hospital, Department of Medical Oncology
2009–2011	Specialist in Trakya University Hospital, Department of Medical Oncology
2011–2015	Assistant Professor in Trakya University Hospital, Department of Medical Oncology
2015–2019	Assoc. Professor in Trakya University Hospital, Department of Medical Oncology
2019–Present	Professor in Trakya University Hospital, Department of Medical Oncology

Membership:
Medical Oncology Society

Publications:

1. Cicin, I., H. Karagol, S. Uzunoglu ve K. Uygun, "Efficient and safe application of a FOLFIRI/bevacizumab combination to a patient with locally advanced rectal cancer and severe chronic renal failure," Onkologie, 30(1-2), 65 (2007).
2. Cicin, I., H. Karagol, S. Uzunoglu, K. Uygun, U. Usta, Z. Kocak, M. Caloglu, M. Saynak, F. Tokatli ve C. Uzal, "Extrapulmonary small-cell carcinoma compared with small-cell lung carcinoma: a retrospective single-center study," Cancer, 110(5), 1068-1076 (2007).
3. Kocak, Z., M. Saynak, F. Oz-Puyan, I. Cicin, R. Cosar-Alas, M. Caloglu, G. Altiay ve S. Uzunoglu, "Inguinal lymph node as the only evidence of progressive lung Cancer," Rev Port Pneumol 14(5), 709-713 (2008).
4. Uygun, K., G. Aksu, I. Cicin, H. Karagol, Z. Kocak, M. Fayda, A. Binici ve S. Uzunoglu, "The efficiency of single agent docetaxel in patients with platinum-refractory non-small cell lung carcinoma," Med Oncol, 25(4), 408-414 (2008).
5. Cicin, I., F. Ozyilmaz, H. Karagol, F. Yalcin, S. Uzunoglu ve Kaplan M, "Massive Upper Gastrointestinal Bleeding From Pure Metastatic Choriocarcinoma in Patient with Mixed Germ Cell Tumor with Subclinical Intestinal Metastasis," Urology, 73(2), 443.e15-7 (2009).
6. Cicin, I., U. Usta, H. Karagol, S. Uzunoglu ve Z. Kocak, "Extrapulmonary small cell carcinoma localized in lymph nodes: Is it a different clinical entity?," Acta Oncol, 48(3), 354-360 (2009).
7. Cicin, I., U. Usta, A. Sezer, S. Canbaz, S. Uzunoglu, H. Karagol ve A. S. Karasalihoglu, "Synchronous Tonsil, Gallbladder and Cardiac Metastasis without Other Visceral Metastases of Malignant Melanoma," Onkologie 32(4), 197-199 (2009).
8. Cicin, I., H. Karagol, U. Usta, A. Sezer, S. Uzunoglu, R. Alas-Cosar, T. Yetisyigit ve K. Uygun, "Triple Negative Breast Cancer Compared to Hormone Receptor Negative/HER2 Positive Breast Cancer," Med Oncol, 26(3), 335-343, (2009)
9. Ozen, A., I. Cicin, A. Sezer, S. Uzunoglu, M. Saynak, H. Genchellac ve H. Karagol, "Dural sinus vein thrombosis in a colon cancer patient treated with FOLFIRI/Bevacizumab," J Cancer Res Ther, 5(2), 130-132 (2009).
10. Uygun, K., A. Bilici, H. Karagol, M. Caloglu, I. Cicin, G. Aksu, M. Fayda ve S. Uzunoglu, "The comparison of weekly and three-weekly cisplatin chemotherapy concurrent with radiotherapy in patients with previously

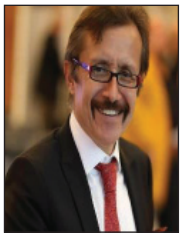
untreated inoperable non-metastatic squamous cell carcinoma of the head and neck," Cancer Chemother Pharmacol, 64(3), 601-605 (2009).
11. Cosar R., C. Uzal, F. Tokatli, B. Denizli, M. Saynak, N. Turan, S. Uzunoglu, A.Ozen, A.Sezer, K. Ibis, B. Uregen, V. Yurut-Caloglu, Z. Kocak, "Postmastectomy irradiation in breast in breast cancer patients with T1-2 and 1-3 positive axillary lymph nodes: is there a role for radiation therapy?" Radiat Oncol, 30, 6:28 (2011)
12. Uzunoglu S., H. Karagol, F. Ozpuyan, R. Cosar, I. Cicin, V. Yurutcaloglu, B. Denizli, Ö.Tanriverdi, N. Sut, Z. Kocak, "Protective effect of L-carnitine versus amifostine against cisplatin-induced nephrotoxicity in rats. Med Oncol. 28, 690-696,2011
Presentations:
1. K Uygun, H Karagol, M Caloglu, I Cicin, V Yurut-Caloglu, S Uzunoglu, P Saip. The comparison of weekly and 3-weekly cisplatin chemotherapy concurent with radiotherapy in patients with previously untreated inoperable non-metastatic SCCHN. 31st ESMO Congress, 29 September - 3 October 2006, İstanbul, Turkey. Annals of Oncology, 17(Supplement 9):ix182,2006
2. Uygun, K., I. Cicin, H. Karagol, P. Saip ve S. Uzunoglu, "Second line chemotherapy non small cell lung carcinoma: A single-institution experience" 31st The European Society for Medical Oncology Congress, Istanbul, Vol. 17, suppl 9, 239, Poster sunu 812, Annals of Oncology, 2006.
3. Uygun, K., I. Cicin, H. Kargol, S. Uzunoglu, Z. Kocak, M. Caloglu ve P. Saip, "The treatment results of patients with extra-pulmoner and pulmoner small cell Cancer," 31st The European Society for Medical Oncology Congress, Istanbul, Vol. 17, suppl 9, 240, Poster sunu 816, Annals of Oncology, 2006.

Ömer Dizdar
Hacettepe University Cancer Institute, Ankara, Turkey

2000	Degree in Medicine, Hacettepe University
2000–2005	Residency in Internal Medicine, Hacettepe University
2005–2009	Residency in Medical Oncology, Hacettepe University
2011–2017	Associate Professor in Medical Oncology – Baskent University (2011–2014); Hacettepe University Cancer Institute (2014–2017)
2015–2017	Master degree in Cancer Epidemiology
2018–present	Professor in Medical Oncology – Hacettepe University Cancer Institute

Areas of scientific interest:
Breast cancer
Gastrointestinal cancer
Membership:
Turkish Society of Medical Oncology
European Society of Medical Oncology
Major publications:
1. Aktas BY, Guner G, Guven DC, Arslan C, Dizdar O. Exploiting DNA repair defects in breast cancer: from chemotherapy to immunotherapy. Expert Rev Anticancer Ther. 2019 Jul;19(7):589-601.
2. Guven DC, Dizdar O, Alp A, Akdoğan Kittana FN, Karakoc D, Hamaloglu E, Lacin S, Karakas Y, Kilickap S, Hayran M, Yalcin S. Analysis of Fusobacterium nucleatum and Streptococcus gallolyticus in saliva of colorectal cancer patients. Biomark Med. 2019 Jun;13(9):725-735.
3. Sahin T, Dizdar O, Ozdemir N, Zengin N, Ates O, Oksuzoglu B, Sendur MAN,Bilgin B, Demir M, Bozbulut UB, Kilickap S, Yalcin S. The frequency and predictors of persistent amenorrhea in premenopausal women with colorectal cancer who received adjuvant chemotherapy. Anticancer Drugs. 2019 Mar;30(3):289-294.
4. Karakas Y, Dizdar O, Aksoy S, Hayran M, Altundag K. The Effect of Total Sizeof Lesions in Multifocal/Multicentric Breast Cancer on Survival. Clin Breast Cancer. 2018 Aug;18(4):320-327.
5. Dizdar O, Ozçakar L, Malas FU, Harputluoglu H, Bulut N, Aksoy S, Ozisik Y, Altundag K. Sonographic and electrodiagnostic evaluations in patients with aromatase inhibitor-related arthralgia. J Clin Oncol. 2009 Oct 20;27(30):4955-60.

Ismail Celik
Hacettepe University Cancer Institute, Ankara, Turkey



He is an internist and medical oncologist. He also has MS degree in cancer epidemiology. He worked as a visiting NCI scholar in the Johns Hopkins University between 2006-2007.
He is the director of the "Turkish Immunotherapy and Oncology Association" and President-Elect of the Turkish Society of Medical Oncology.
His field of interests are melanoma and immunotherapy and he currently works at the Hacettepe University Cancer Institute, Ankara.

Kivilcim Eren Erdogan
Çukurova University

Education:

2001–2007	Hacettepe University School of Medicine
2007–2011	Cukurova University Faculty of Medicine, Department of Pathology

Current position:
Çukurova University Faculty of Medicine Balcali Hospital, Department of Pathology
Professional experience:

2007–2011	Cukurova University Faculty of Medicine, Department of Pathology Residency in Surgical Pathology
2012–2015	Mersin State Hospital Department of Pathology. Specialist of Pathology
2015–2018	Cukurova University Faculty of Medicine, Department of Pathology (Surgical Pathologist)
2018–	Assistant professor Cukurova University Faculty of Medicine, Department of Pathology (Surgical Pathologist)
2019	Internship at Pathology Department of Rizzoli Orthopedic Oncology Hospital, Bologna, Italy

Experience:
Experience on musculoskeletal pathology
Publication:
Residency Thesis: Evaluation of epidermal growth factor receptor in odontogenic tumors and rare soft tissue tumors by immunohistochemical and fluorescence in situ hybridization methods
Articles
Duzgun O, Sarici IS, Gokcay S, Ates KE, Yilmaz MB. Effects of nivolumab in peritoneal carcinomatosis of malign melanoma in Mouse model. Acta Cir Bras 2017;32(12):1006-1012.
Yakan, S., Dağlıoğlu, Y.K., Erdoğan, K.E. The protective effects of hypericum perforatum and nigella sativa on testicular tissue after testicular torsion and detorsion. 2018 International Journal of Applied Research in Veterinary Medicine
Şahin M, Karayakar F, Erdogan KE, Bas F, Colak T. Liver tissue trace element levels in HepB patients and the relationship of these elements with histological injury in the liver and with clinical parameters. J Trace Elem Med Biol. 2018 Jan;45:70-77. doi: 10.1016/j.jtemb.2017.09.014.
Kaplan HM, Şingirik E, Erdoğan KE, Doran F. Protective effect of alpha-linolenic acid on gentamicin-induced ototoxicity in mice. Somatosens Mot Res. 2017 Sep;34(3):145-150. doi: 10.1080/08990220.2017.
Deveci MA, Özbarlas HS, Erdoğan KE, Biçer ÖS, Tekin M, Özkan C. Elastofibroma dorsi: Clinical evaluation of 61 cases and review of the literature. Acta Orthop Traumatol Turc. 2017 Jan;51(1):7-11. doi: 10.1016/j.aott.2016.10.001.
Erdogan KE, Deveci MA, Paydas S, Gonlusen G. Morphologic evaluation of the effect of denosumab on giant cell tumors of bone and a new grading scheme. Pol J Pathol. 2016;67(4):392-397. doi: 10.5114/pjp.2016.65873.

Rencüzoğulları A, Erdoğan KE, Sarıtaş AG, Topal U, Akçam AT, Ülkü A, Yalav O, Eray İC, Dalcı K, Doran F. İntraabdominal ekstragenital yerleşimli endometriozisler: tek merkez deneyimi. Cukurova Med J 2018;43(2) Doi: 10.17826/cumj.370849.
Türkmen İÇ, Usubütün A, Çakir A, Aydin Ö, Bolat FA, Akbulut M, Altinay S, Arici S, Aslan F, Astarci M, Bağir EK, Baş Y, Başsüllü N, Çelik B, Çetiner H, Çobanoğlu B, Aydin A, Demir H, Doğan HT, Eken KG, Erhan SŞ, Erdoğan G, Erdoğan KE, Eren F, Ersöz Ş, Firat P, Gürses İ, Haberal N, Kahraman DS, Kamali GH, Karabulut YY, Kefeli M, Koyuncuoğlu M, Köseoğlu RD, Müezzinoğlu B, Onal B, Önder S, Özcan Z, Kimiloğlu E, Özer H, Sönmez FC, Şahin S, Şahin N, Yalta T. What does the Data of 354,725 Patients from Turkey Tell Us About Cervical Smear Epithelial Cell Abnormalities? - The Epithelial Cell Abnormality Rate is Increasing - Quality Control Studies and Corrective Activity are Musts. Turk Patoloji Derg. 2017;33(2):134-143. doi: 10.5146/tjpath.2016.01380.
Erdoğan KE, Deveci MA, Gönlüşen G, Uğuz A, Ergin M, Dinigüzel Ö, Özbarlas S. Yumuşak dokunun nadir görülen tümörlerinde ve odontojenik tümörlerde immünohistokimyasal yöntem ve floresan in situ hibridizasyonla epidermal growth faktör reseptör varlığının gösterilmesi. Cukurova Med J 2016;41(2):316-325. DOI: 10.17826/cutf.209059.
Kösemehmetoğlu K, Tan A, Esen T, Ateş KE. Asistanların bakışı ile Türkiye'de patoloji uzmanlık öğrencisi eğitimi: bir anket çalışması. Turk Patoloji Derg. 2010;26(2):95-106.
Akçalı M, Yapıcıoğlu H, Akay E, Özlü F, Kozanoğlu B, Erdoğan K, Gönlüşen G, Satar M. A congenital soft tissue Ewing sarcoma in a newborn patient. Turk J Pediatr. 2017;59(1):76-79. doi: 10.24953/turkjped.2017.01.013.
Kelle B, Polat Kelle A, Erdogan KE, Kozanoglu E. A rare cause of shoulder pain: monostotic fibrous dysplasia. Arch Rheumatol 2016;31(2):184-187. Doi: 10.5606/ArchRheumatol.2016.5828
Iflazoğlu N, Mirili C, Karaalioğlu B, Duran A, Çapkınoğlu E, Parsak CK, Erdoğan KE, et al. Primary Colon Lymphoma Presenting with Obstructive and Hemorrhagic Symptoms. DOI: 10.4274/tjcd.galenos.2018.46762 Turk J Colorectal Dis 2019;29:61-64.
Sarıtaş, A.G., Doran, F., Erdoğan, K, et al. Pancreatic lymphangioma: A rare case report. 2019 Haseki

Paul Szabolcs
Children's Hospital of Pittsburgh

Trained at Semmelweis University School of Medicine in Budapest. He completed pediatric residency at Bellevue Hospital/NYU Medical Center. He trained in Hem-Onc at Memorial Sloan Kettering Cancer Center (MSKCC) in New York. He pursued post-doctoral fellowship at MSK in Molecular Biology at Rockefeller University in Physiology and Cellular Immunology. He has launched and led the BMTCT division at the Children's Hospital of Pittsburgh since 2011 following 13 years at Duke University where he received tenure studying the immunobiology of cord blood transplantation. His current laboratory interns focus on elucidating mechanisms of tolerance after HLA mismatched cord blood and bone marrow transplantations. He is leading efforts to utilize HJCT to promote tolerance after solid organ transplantation.

Patrick Schlegel
Universitätsklinikum Tübingen, Tübingen, Germany

Born in Tanzania 1981

2002–2008	Studied Medicine at the Eberhard Karls University in Tübingen
2009–2017	Training of Pediatrics in Tübingen
2012–2017	PostDoctoral Researcher/Clinician Scientist, Mentors: Peter Lang, Rupert Handgretinger
2017–2019	Training for Pediatric Hematology/Oncology and Stem Cell Transplantation in Tübingen, Mentors: Peter Lang, Rupert Handgretinger

Clinical training in allogeneic HSCT and pediatric immunotherapy >5 years
Affiliations:

2019	Consultant physician Pediatric Hematology/Oncology and Stem Cell Transplantation, University Children's Hospital Tübingen
2019	Head of CAR-T cell Laboratory and CAR-T cell development program of the iFIT Cluster of Excellence, University Hospital Tübingen

Main focus of clinical work: a) allo HSCT and b) cellular as well as humoral immunotherapy in pediatric cancer
Main focus of scientific work: Adapter CAR-T cell development and clinical translation (AML), CAR-T cell tuning in solid cancer

Selim Çorbacıoğlu
Children's Hospital in Regensburg, Germany

Selim Corbacioglu is Professor and Chair of the Department of Hematology, Oncology and Stem Cell Transplantation at the Children's Hospital in Regensburg, Germany. Professor Corbacioglu's research interest is focused on curative options for hemoglobinopathies, and transplant-related systemic endothelial complications such as VOD/SOS and PRES. He was the PI of the multicentre defibrotide prevention trial in children and is the PI for a prospective international trial to evaluate haploidentical HSCT as a curative option for patients with sickle cell disease. The recipient of the Van Bekkum Award of the EMBT in 2010, Professor Corbacioglu is the author or co-author of numerous peer-reviewed articles published in Lancet, *Blood*, *Leukaemia* and *Bone Marrow Transplantation* among others and the current chair of the Pediatric Disease Working Party of the EBMT.

Malek Baassiri
Makassed General Hospital, Beirut, Lebanon

Dr. Malek Baassiri, Pediatric Hematologist/Oncologist, Pediatric Cancer Survivors Specialist, and Bone marrow transplant specialist at Makassed General Hospital, Beirut, Lebanon. Received his medical degree from Beirut Arab University (BAU) in 2008 and completed a residency in Pediatrics at Hammoud Hospital University Medical Center, Lebanon, in 2012, followed by fellowship training in Hematology-Oncology at the American University of Beirut Medical Center in 2015, then fellowship training in Pediatric cancer survivors at St. Jude Children's Research Hospital (SJCRH), USA, and finally, BMT training at Medical Park Hospital, Antalya, Turkey.
Understanding the need for additional specialized training, Dr. Baassiri successfully applied for the Cancer Conquer Foundation-American Society of Clinical Oncology Long-Term International Fellowship Award 2015 and was awarded additional training in survivorship and outcomes research under the mentorship of Dr. Melissa Hudson at SJCRH, Memphis USA.
At St. Jude Children's Research Hospital, he had the unique opportunity to collaborate with multidisciplinary investigators on a variety of late effects projects as well as to lead an analysis investigating outcomes among survivors of Acute Myeloid Leukemia participating in the St. Jude Lifetime Cohort Study. In addition to these research experiences, Dr. Baassiri acquired skills in clinical data management needed for the development of an academic long-term follow-up program.
Dr. Baassiri, is currently the head of the divicion of Pediatric Hematology-Oncology at Makassed Genreral hospital, Beirut, is a member of the American Society of Clinical Oncology (ASCO), Pediatric Oncology East and Mediterranean Group (POEM), and an international associate of the Children Oncology Group (COG), Dr. Baassiri has multiple publications in peer reviewed journals. Moreover, he is involved in teaching BAU medical students

and residents in the field of pediatric hematology and oncology. In 2018, he became a legal expert in the Lebanese courts.

Lalith Parmar
Sankalp India Foundation an NGO

He is President and volunteer of Sankalp India Foundation an NGO that is working for the cause of Blood Donation, Thalasemia Management and Cure. He is an Telecom Engineer by profession and is currently Co-Founder of Jagriti innoHealth Platforms a health care technology company. In the last 13 years with Sankalp, he has been involved from organising blood donation drives to setting up of bone marrow transplant and Thalassemia management centres in India. His primary responsibility now is fundraising for the organisation and expansion of care centres. Lalith is passionate about working towards a Thalassemia Free India.

Şule Ünal
Hacettepe University, Ankara, Turkey

Dr. Unal has graduated from Hacettepe University Faculty of Medicine (English) in 1999. She received her speciality in Child Health and Diseases in 2005. She completed Pediatric Hematology subspeciality in 2010 and became Assoc. Prof. of Pediatrics in 2011 and Prof of Pediatrics in 2017.
Dr. Unal had clinical and laboratory experience in Texas Children's Hospital, USA in 2009. She made country service between 2011 and 2012 in Antakya State Hospital. Currently, Dr Unal is working as Professor of Pediatrics, in Hacettepe University, Department of Pediatric Hematology in Ankara, Turkey and is the Director of Center for Fanconi Anemia and Other Inherited Bone Marrow Failure Syndromes İn Hacettepe University. She has Turkish Society of Hematology Young Investigator Award, Novartis Industry, Bayer-Schering Pharma Industry, TSH-TURKBA Awards. In 2015 she received ASCO-IDEA Award. She is currently the President of Congenital Blood Disorders, Treatment and Support Association and Board Member of Turkish Society of Pediatric Hematology. She is at present the Assoc. Editor of Turkish Journal of Hematology, Hematology Section Editor of Turkish Journal of Pediatrics and managing editor of Acta Medica.
She has ECFMG, Strategic Planning, Improvement Teams-Guide Training certifications.
Her professional interest is the field of hemoglobinopathies and inherited bone marrow failure syndromes

Rose Ellard
Royal Marsden Hospital

I am a registered nurse and currently working as a Lecturer Practitioner at the Royal Marsden Hospital within the Royal Marsden School. Prior to this role I worked as a research nurse for many years, my most recent role being in the field of CAR-T. I have an MSc in Advanced Practice (Cancer) and have presented at a number of national and international conferences and study days on CAR-T therapy. I am also the nurse member of the EBMT Cellular Therapy and Immunobiology Working Party and I am currently working on the development of CAR-T guidelines for nurses.

Erik Aerts
University Hospital Zürich, Switzerland

Erik Aerts is President of the Scientific Committee of the Haematology Nurses & Healthcare Professionals Group. He has been involved in EBMT Nurses Group since 1994 when he first joined the EBMT Nurses Group. Erik Aerts then began work on creating the Swiss EBMT Nurses Group, of which he served as President from 2004–2006.
In November, 2005, he developed and led the first Haematology-Oncology Nursing module in Switzerland, which supports nurses and gives them the opportunity to specialise in the field of haematology.
He is currently involved in organising and teaching educational study days for several haematology and oncology projects. He also has a special interest in projects for the improvement of patient care. Since 1998 he has been the Nurse Manager of the BMT/SCT ward and since 2009 the Nurse Manager of the Polyclinic Haematology of the University Hospital Zürich, Switzerland.
In total he has 30 years of nursing experience in a wide variety of settings and specialties, focusing on haematology and haematopoietic stem cell transplantation (HSCT).
The Haematology Nurses & Healthcare Professionals Group has been established in 2014 and registered in Switzerland. The Haematology Nurses and Healthcare Professionals Group has been established to support nurses and other health care professionals through the rapidly evolving landscape of haematology and enable them to deliver optimal care to patients and support their families.
The Haematology Nurses and Healthcare Allied Professionals Group (here after referred as to "HNHCP") is a non-profit organisation. The HNHCP is an international organization dedicated to charitable, educational and scientific purposes. The members of the HNHCP Group are qualified nursing staff and allied healthcare professionals from centers/institutions caring for and working with patients who have haematological disorders both malignant and non-malignant including haemaglobinopathies, coagulation and thrombotic disorders. Members also include cancer nursing organizations, organisations, institutions, pharmaceutical companies, agencies and other professionals involved in or interested in the care of haematology patients.
We invite individual nurses, healthcare professionals and societies/organisations to join the group in supporting and developing professional care of haematology patients and their carers. If you would like to become a member, or would like more information, please visit the homepage of the Haematology Nurses and Healthcare.

Fatih Erbey
Koç University School of Medicine, İstanbul, Turkey

Associate Professor Doctor M. Fatih Erbey was born in 1976 in Gaziantep. He graduated from Gaziantep High School in 1993 and from Çukurova University Faculty of Medicine in 1999. He completed his pediatric residency training in 2005 and Pediatric Oncology training in 2009 at Çukurova University Faculty of Medicine. In 2007, he was as an Observer physician at Pediatric Bone Marrow Transplantation Unit, Pittsburgh Children's Hospital, in the USA. In 2009–2010 he fulfilled her state service obligations in Van Maternity and Children Hospital. In 2011, he worked as a faculty member in the Pediatric Oncology and Bone Marrow Transplantation Unit of Ege University Faculty of Medicine. Between 2011–2014, he worked in the Pediatric Hematology/Oncology and Bone Marrow Transplantation Unit of Medicalpark Bahçelievler Hospital and, in 2014–2018, he worked in the Pediatric Hematology/Oncology and Bone Marrow Transplantation Unit of Acıbadem University School of Medicine. He became an Associate Professor in 2013. Assoc. Prof. Dr. M. Fatih Erbey has been working as a lecturer in Koç University School of Medicine since March 2019. He is also working as a Pediatric Hematologist/Oncologist in VKV Health Institutions.

Marjola Gjergji
Bambino Gesù Children's Hospital in Rome

Work experience:
Pediatric RN in Oncohaematology and Bone Marrow Transplant Department (BMT).
I assist patients undergoing CAR-T Cell treatments. In collaboration with the medical team, I draft protocols on the prevention and ongoing treatments of genitoperianal lesions in pediatric oncohematological patients.
Active member of the hospital nursing research group.
Providing inpatient nursing care and executing interventions through planning, management and evaluation by following up to date literature and hospital policies; not limited to the administration of chemotherapy and the management of central lines.
In collaboration with medical staff and various healthcare professionals, I assist in programming individualized oncohematological patient careplans.
Providing emotional support to patients and their families by educating them about their diseases in hospital and after discharge care
Asses and provide care of patients with serious respiratory disorders including patients after lung transplants
Education:

2012–2013	Master Degree in Critical Care of Nursing. Nurse anesthetist, emergency, ambulance, BLSD, P-BLSD, ALS, cardiosurgery, neurotraumatology, stroke, Intensive Care Unit, Trauma Surgery Unit, Nursing training
2009	Stage for thesis degree: Radiation Therapy in Pediatry
2006–2009	Degree in Nursing, Nursing training. Thoracic surgery, general surgery, gastroenterology, cardiology, pediatric oncology, neurosurgery, intensive care

Certifications:

02/2019	1st European CAR T- Cell Meeting, Paris
15/10/2018	Care pathway for a teenager with cancer, OPBG Rome
09/2018	European Pressure Ulcer advisory Pannel (EPUAP) 2018, Rome
06/2018	EBMT 11TH PDWP, IDWP, IEWP& 6th Nurses Group Meeting, Verona
05/2018	XLIII National Meeting AIEOP, Bologna
03/2018	44th EBMT Annual Meeting, Lisbon
03/2018	Abnormalities and skin lesions, mucosa and endothelium in HSCT, Rome
02/2017	Clinical Tutoring for students in nursing, Rome
2017	Wound Care in Pediatry, Rome
10/2017	Biological drugs in pediatric oncohematology, Rome
02/2017	BLS AHA, Rome
05/2016	Taking care of the end of the life/palliative care/bio-ethics, Rome
12/2015	G.A.L.I.E.O. scientific evidence based and clinical practice, Rome
06/2013	XXXVII National Meeting AIEOP, Roma

Awards:
Incontinence associated dermatitis (IAD) and perianal septic lesions in children with oncohematological diseases. Results of a protocol applied for IAD systemic prevention and early treatment 146 patients later", EPUAP &3M Pressure Ulcer and IAD Innovation Awards at 20th Annual Meeting of the EPUAP, 12-14/09/18, Rome
Speaker:
"Haploidentical TX; parents as donors", speaker at EBMT 11TH PDWP,IEWP& 6TH Nurses Group Meeting, 06-09/06/18
"Mortality and Morbidity in OPBG" speaker at XXXVII National Congress AIEOP, 10/06/13, Rome
Bio:
Marjola Gjergji is a pediatric RN at Bambino Gesù Children's Hospital in Rome. She graduated in 2009 from the University "La Sapienza" in Rome with Bachelor Degree in Science of Nursing. During her studies she gained extensive experience in the nursing field with particular attention IN pediatric oncology. In fact, to develop the thesis topic, Marjola did an internship at the CRO, Oncology Center in Aviano (IT) for the purpose of developing her thesis topic in radiation therapy in oncohematologic children.
After graduation, she worked for the "Dynamo Camp", no profit association which promotes and manages holiday camps by hosting children suffering from serious and chronic diseases. In 2010 she started working at the "Policlinico Umberto I" Hospital in Rome in the department of pediatrics, managing children with cystic fibrosis.
In 2011 she stared working at the Bambino Gesù Children's Hospital in Rome in the department of Oncohematology and BMT Unit, where she is currently working. In 2012 Marjola completed master's degree in Rome in Critical Care of Nursing. After a long experience with oncohematological patients, she's currently working at the BMT Unit with particular attention to children treated with Car-T cell. She works closely with the Nursing Research Group and Pediatric Skin Care Team.
Recently, she has become a member of the EBMT Nursing Group committee. She is currently working on a project in prevention and treatment of IAD in Oncohematology patients which in 2018 was awarded at the 20th EPUAP Annual Meeting in Rome.

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Abstracts of the Xth Eurasian Hematology Oncology Congress 8–11 October 2019, Istanbul, Turkey

Speaker Presentations

SP-01
Current treatment of acute promyelocytic leukemia

Miguel A. Sanz
Hospital Universitario La Fe and Department of Medicine of the Universitat de Valencia, Valencia, Spain

Since the introduction of all-trans-retinoic acid (ATRA), the use of this molecularly targeted treatment in combination with anthracycline-based chemotherapy has completely changed the prognosis of acute promyelocytic leukemia (APL), turning it into the most curable myeloid leukemia. Also, the use of risk-adapted protocols during the past two decades has contributed to optimize the drug combination and the most appropriate dose intensity for each subset of patients classified according to both risk of relapse and vulnerability to drug toxicity. After the outstanding results with arsenic trioxide (ATO) in the treatment of APL relapse, recent developments have included the investigation of the role of ATO as front-line treatment, both to minimize or even omit the use of cytotoxic agents and to improve the outcome of the conventional chemotherapy-based approach. In this presentation, most recent advances in the treatment of patients with newly diagnosed and relapsed APL will be discussed, particularly considering the latest developments with the use of ATO-based regimens as targeted first-line treatment without chemotherapy.

SP-02
Precision medicine for CML

Giuseppe Saglio
Department of Clinical and Biological Sciences of the University of Torino and Ospedale Mauriziano, Torino, Italy

Chronic myeloid leukemia (CML) is likely to represent in modern medicine the most successful achievement of the so-called targeted therapy and precision medicine. Since the discovery of the Philadelphia chromosome and of its closer association with this specific disease, a continuous flow of biological and clinical research has progressively provided insights on the CML pathogenesis of and on mechanisms leading to its progression to an acute phase, that until two decades ago was the major cause of death for the CML patients. This situation totally changed since the introduction of imatinib, the first tyrosine kinase inhibitor (TKI) introduced in clinical medicine. Several studies indeed suggest that after 10 years from the start of therapy, the OS of the CML patients is almost overlapping that of a control population without leukemia. These results however are not only due to imatinib, but also to other TKIs of second and third generation like nilotinib, dasatinib, bosutinib, radotinib, ponatinib and others. These TKIs are generally used as second or third line treatment in cases (approximately 35-40% of all patients) who are intolerant or resistant to imatinib therapy, but nilotinib, dasatinib and bosutinib have been used and registered also as first line therapy in the attempt to improve the first-line therapy results that can be obtained with imatinib. The decision to change therapy is based on the molecular quantification by quantitative RQ PCR of the amount of the BCR/ABL transcript at specific time points that is corresponding to the amount of the residual disease. The selection of the TKI to be used as first- or second-line therapy is also in many cases established based on the profile of the BCR-ABL mutation present. In other cases, is the toxicity profile of each TKI the factor determinant for the choice. The enormous success of the TKI therapy however should not overshadow the fact that most of them are bound to continue the TKI therapy for the rest of their life. Therefore, the new frontier of the CML therapy is represented by the treatment free remission (TFR) that means that the patient can discontinue the TKI therapy without experiencing a relapse of the disease. This in the net year will certainly represent a new challenge in which the so-called precision medicine will play a major role.

SP-03
Precision medicine in MDS

Mustafa Cetiner
Acibadem Maslak Hospital, Department of Hematology

Precision medicine in MDS (myelodysplastic syndrome) aims to personalize treatment based on each patient's features to provide maximum benefit and minimize the toxicity. In the recent years, advances in genomics and next generation sequencing (NGS) have offered an opportunity to use of patients' genetic profiles and MDS related somatic mutations for the diagnosis, risk stratification and prediction of treatment response.

MDS is a very heterogenous disease characterized by impaired hematopoiesis resulting in cytopenia and dysplasia. Originating from its heterogeneity, overall survival of patients ranges from months to years. Most commonly used tool for risk stratification "International Prognostic Scoring System Revised (IPSS-R)" has a limitation to predict survival particularly for low- and intermediate- risk MDS patients. IPSS-R incorporates cytopenia, bone marrow blast percentage and specific cytogenetics abnormalities, but not molecular markers.

To date, 40 different somatic mutations have been identified in MDS. Approximately 80–90% of MDS patients exhibit at least 1 genetic abnormality including both chromosomal anomaly and somatic mutations.

There are several studies that showed incorporation of specific molecular markers into scoring system provides more accurate risk prediction for MDS patients.

Several studies revealed that presence of TP53, ASXL1, NRAS, SRSF2 and EZH2 is associated with worse prognosis and SF3B1 mutation is the only somatic mutation related with better outcomes.

TP53 mutations account for nearly 25% of high-risk MDS and 50% of treatment related MDS/AML cases. 90% of patients with TP53 mutation comprise complex karyotype (CK). TP53 mutation has strongly negative effect

on prognosis even after allogenic stem cell transplantation. Recently, it has been revealed that patients with TP53 mutation have higher response rates to hypomethylating agents (HMA) especially to Decitabine. HMA as a bridging treatment to stem cell transplantation may offer a promising therapy option to reduce tumor burden for this dismal group.

A group of genes associated with DNA methylation and chromatin modification called TET2, DNMT3A and ASXL1 are mutated in up to 60–70% of MDS patients. Although ASXL1 is known for negative impact on outcome, there are conflicting findings for DNMT3A and TET2 mutations. In 2017, a meta-analysis that scrutinized the prognostic role of TET2 mutation in MDS suggested no significant prognostic value of TET2 deficiency on MDS. On the other hand, some studies pointed out higher response rate to HMA among MDS patients with TET2 or DNMT3A mutation. It is important to remember that these mutations' role on treatment success is not clear-cut.

Mutation of another DNA methylation gene "Isocitrate dehydrogenase (IDH-1/2)" is prevalent among 5% of MDS patients. "Inosidenib and Enasidenib" -selective IDH1 inhibitor and IDH2 inhibitor respectively- has been approved by FDA for the treatment of adults with relapsed or refractory AML in 2018. Preliminary results for MDS patients are encouraging to date with overall response rates of 50%. On the other hand, very low prevalence rates of IDH 1/2 mutations in MDS contrary to AML raise a question for the convenience of IDH inhibitors among MDS patients.

Another gene class of somatic mutations involving SF3B1, SRSF2, U2AF1 and ZRSR2 which collectively exist among 50% of MDS patients is splicing factors. SF3B1 mutation is strongly correlated with specific sideroblastic phenotype, found in 64–90% of patients with ring sideroblasts (RS). Studies revealed that positivity of SF3B1 mutation predicts favorable prognosis. Patients aged 70 years or older with refractory anemia with ring sideroblast (RARS) have a normal life expectancy compared with general healthy population.

Luspatercept (ACE-536) that promotes late stage erythroid differentiation has been shown to be effective for treatment of patients with RS and SF3B1 mutation in Phase 3 MEDALIST trial in 2018. FDA approval of the drug is expected by 2020 and Luspatercept may offer a hope for this specific group of patients in the future.

Another splicing factor "SRSF2" mutation which accounts for worse outcome in MDS is the most common mutation in CMML patients, in which TET2 and ASXL1 mutations co-exist in 50% of cases. However, meta-analysis conducted in 2018 suggested no prognostic impact of SRSF2 mutation on CMML patients concluding with its unclear role on management of these patients in the real world.

In conclusion, two somatic mutations TP53 and SF3B1 warrant a noteworthy consideration in clinical practice due to their prognostic significance. Special and more aggressive approach should be given for patients with TP53 mutation due to their increased risk of AML evolution.

To date, somatic mutations have relatively minor effect on treatment selection in daily practice, except for clinical trials. The role of molecular markers on clinical phenotype, prognosis and as well as pathogenesis of MDS remains to be clarified. Further studies and clinical trials need to be carried out for treatment selection and development of targeted treatment for MDS patients.

References

[1] Ogawa S. Genetics of MDS. Blood 2019;133(10):1049–59.
[2] Sallman DA, Komrokji R, Vaupel C, et al. Impact of TP53 mutation variant allele frequency on phenotype and outcomes in myelodysplastic syndromes. Leukemia 2016;30:666–73.
[3] Kuendgen A, Müller-Thomas C, Lauseker M, et al. Efficacy of azacitidine is independent of molecular and clinical characteristics-an analysis of 128 patients with myelodysplastic syndromes or acute myeloid leukemia and a review of the literature. Oncotarget 2018;9(45):27882.

SP-04

The use of BMT with malignant lymphomas: practical issues based on St. Petersburg hematological center experience

Natalia Mikhailova
Raisa Gorbacheva memorial Research Institute for Pediatric Oncology, Hematology and Transplantation, Pavlov First St. Petersburg State Medical University, St. Petersburg, Russia

The majority of lymphoma patients could be cured by standard first line chemotherapy with inclusion of new target agents where available. Additional subset of patients could benefit with high-dose chemotherapy and auto HSCT. Nevertheless, about 30% of patients became refractory or relapsed and could not be cured by chemotherapy approach. Various immunotherapy options are considered as an alternative treatment in such patients: checkpoint inhibitors, monoclonal antibodies (immune conjugates and bispecific), CAR-T cell therapy, alloHSCT and their combinations. AlloHSCT is considered the only potentially curative approach. The problem is the induction of remission before alloHSCT. The best chances have Hodgkin lymphoma patients due to introduction into clinical practice checkpoint inhibitors and brentuximab vedotine(BV). We used these two agents as bridge to alloHSCT.

The results of alloHSCT in 86 patients with r/r cHL who had undergone transplant from 2002 to 2018 were evaluated. The analysis included patients (n=54) received the FluBe conditioning and PTCy GVHD prophylaxis. In group A patients (n=20) received bridge therapy with Nivolumab and in group B patients (n=34) received bridge therapy with Brentuximab vedotin or chemotherapy-based bridges. Time from the last Nivolumab administration to alloHSCT was at least 2 months. At the time of analysis, median follow-up was 12 (1–20) months for group A, and 15 (1–64) months for group B. There was no difference in two-year OS (p=0.5) with significantly better EFS (p=0.035) for group A versus group B: 95% and 95% vs 85.3% and 62% respectively. Relapse incidence was 0% for group A versus 26.5% in group B respectively (p=0.04).Cumulative incidence of non-relapse mortality at 2 years was 5.0% and 13.8% in group A and group B, respectively (p=0.5). There was no difference in grade II-IV (45% vs 27%, p=0.23) and grade III-IV (25% vs 13%, p=0.3) aGVHD, as well as extensive chronic GVHD (21% vs 28%, p=0.83) in groups A and B, respectively.Ten patients in general group (n=86) with relapse after alloHSCT were treated with different doses (0.5–3 mg/kg) of nivolumab in our clinic. At the median follow up of 16 mo (0.6–28) all patients remain alive. The objective response to therapy was assessed in 7 patients noted in all patients (100%), disregard the dose of the nivolumab: CR in 29%, and PR in 71%. The response was lost in four patients, which required nivolumab retreatment. None of the patients developed extensive GVHD after nivolumab administration. All severe adverse events were resolved after nivolumab discontinuation and glucocorticosteroid treatment. There are currently many questions regarding the role and appropriateness of HSCT after PD-1 blockade.

Our study demonstrates that HSCT after PD-1 blockade is feasible and not associated with higher mortality. We suggest that prior PD-1 blockade should not be considered a contraindication to HSCT in patients with relapsed and refractory Hodgkin lymphoma.

SP-05

Unrelated donorship in Russia: donors' register (Kirov hematological institute)

Maria Loginova
Federal Medical Biological Agency of Russia

Since 2009, the Kirov Registry has been systematically working with bone marrow donors (as of 01/08/2019, the total number of donors was 39,741, of which 46% were male, 53% were female; 43% were regular blood donors, 57% were volunteers from donor actions), since 2013 the Registry has its own Collection Center.

As of 01/08/2019, donors of Kirov Registry carried out 158 donations of hematopoietic stem cells. Every year the number of donations during the activation of donors from the Registry is steadily increasing, including through requests for partially compatible donors (9/10). 95.6% donations

were performed in Kirov Collection Center, 4.4% were carried out in other collection centers.

The use of the created and validated activation model with the employment of the Registry and the Collection Center currently provides the following activation times: the period for sending a sample for confirming HLA typing does not exceed 14 days; activation request sent by the transplant center 1.5–2 months prior to the transplantation is implemented in the specified period of time.

Indicator of the efficiency of the Registry is the number of refusals to donation. During the period from 2013 to 01/08/2019, the Registry received 207 requests for the collection of cellular material: 76% were fulfilled; the remaining 24% were not completed due to a number of reasons.

The efficiency of the Registry is confirmed by the demand for donor resources, the timeliness of activation periods and a relatively low percentage of donation refusals.

SP-06

Hemostasis changes in paroxysmal nocturnal hemoglobinuria

Pierre Toulon

Hematology Department, Pasteur University Hospital, Nice, France

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired hematologic disease caused by a clonal hematopoietic stem cell evolution that manifests with hemolytic anemia, thrombosis, and peripheral blood cytopenias. Etiopathogenesis of PNH is based on acquired mutations that lead to the reduction or absence of glycosylphosphatidylinositol (GPI)-anchored proteins (GPI-APs). Amongst the defective GPI-APs, the loss of CD55 and CD59 complement regulators leads to uncontrolled complement activation that accounts for hemolysis and other PNH manifestations. GPI-AP deficiency is almost always due to somatic mutations in the phosphatidylinositol glycan class A (*PIG-A*) gene, a gene involved in the first step of GPI-APs biosynthesis, even though other causative mutations have recently been discovered. Thrombosis risk is greatly increased in patients with PNH and is the greatest cause of morbidity and mortality in the disease. Actually, thromboembolic events are the most common cause of morbidity and mortality in PNH and account for 40–67% of deaths; 40% of patients having suffered an event before diagnosis and 29–44% of patients suffering at least one event throughout the course of their disease. However, the mechanism underpinning this are far from clear and unlike many other thrombotic disorders, predominantly involves complement-mediated mechanisms. PNH leads to a complex and multifaceted prothrombotic state due to the pathological effects of platelet activation, intravascular hemolysis and neutrophil/monocyte activation. Platelet and endothelial microparticles as well as oxidative stress may play a role. Impaired fibrinolysis has also been observed and may be caused by several mechanisms involving interactions between complement activation, coagulation and fibrinolysis. As many factors may affect thrombosis in PNH, the relative contribution of each mechanism that has been implicated is difficult to quantify.

SP-07

Consideration of new agents for incorporation into treatment guidelines in AML

Alan K. Burnett

The Paul O'Gorman Leukaemia Unit, Glasgow University

Contemporary guidelines for treatment of acute myeloid leukaemia (AML) are currently complicated, first, by the emergence of eight new approved treatments in the last two years, and second, by the uncertainty of where, and in some cases, in what dose and schedule in the overall treatment of AML they would be optimally deployed. There may also be biomarkers which further refine use. Previous guidelines have established that standard of care for induction for recipients of intensive treatment should be daunorubicin at a dose level of not less than 60 mg/m^2, although the requirement to dose above this level is less convincing with the possible exception of benefit for patients with a *FLT3* mutation where there is some evidence of benefit at a 90 mg/m^2 dose. Although alternative nucleosides such as cladrabine or clofarabine have been tested, cytarabine remains the standard with no consistent evidence that higher doses are beneficial. In September 2017 gemtuzumab ozogamicin (GO: mylotarg) was re-approved in combination with 3+7 in a schedule of 3 mg/m^2 on days 1,4 and 7 of induction and as a single 3 mg/m^2 dose in consolidation. An individual patient based meta-analysis of 5 trials in adults where GO was combined with induction chemotherapy, clearly showed an improvement in survival due to a reduction in relapse. The benefit was clearest in the favourable risk subgroup, but also in intermediate but not adverse risk subgroups. The optimal dose and schedule and the need in consolidation requires to be established.

Thirty percent of young and 15% of older patients have a *FLT3* mutation which carries and increased risk of relapse, the extent of which depends on the alleleic ratio, and whether there is an associated *NPM1* mutation. The only currently approved targeted agent for first line treatment in combination with chemotherapy is midostaurin. A similar first-generation inhibitor, lestaurtinib, failed in a similarly large randomised trial, Gilteritinib was approved in November 2018 for relapsed *FLT3.* Other inhibitors (quizartinib, crenolinib) are in advanced stage of development.

Next generation sequencing identified mutations of iso-citrate dehydrogenase (IDH 1&2) in 10–15% of patients. Ivosidenib was approved as monotherapy for relapsed/refractory *IDH1*+ patients was approved in July 2018, and for first line treatment unfit patients >74 years in May 2019. Enosidenib was approved for relapse/refractory IDH2+ in August 2017. None of the registration studies was randomised, so it is unclear if these agents given as monotherapy id superior to chemotherapy. The hope would be to bring these inhibitors into first line treatment in combination with chemotherapy, but this is a considerable statistical challenge since 50% if first remission patients do not relapse on existing therapy.

For older (50–70 years) the liposomal formulation of daunorubicin/ara-C in a fixed 5:1 ratio (Vyxeos), provided a significant survival benefit in high risk patients in a randomised comparison with standard 3+7 treatment, and may represent a step forward for high risk patients and was approved for fist line use in August 2017. A number of studies against other treatments in other settings are underway. A Hedgehog pathway inhibitor (Glasdegib) was approved in November 2018 based on a nonrandomised trial in combination with chemotherapy in untreated older patients and a similar parallel study in combination with low dose Ara-C (LDAC) and a randomised study vs chemotherapy alone are underway. It is probably premature to incorporate glasdegib into guidelines until corroborative studies emerge.

BCL2 overexpression is common in AML, and is associated with poorer outcome and is more frequent in older patients. Previous efforts to target this protein in AML have failed, but venetoclax has encouraged much interest initially in older patients in combination with LDAC or azacitidine or dectibine, where it has achieved importantly higher response rates than either LDAC or DMTs alone, and these responses have been more durable, so these unrandomised studies achieved regulatory approval in November 2018 of venetoclax. Confirmatory randomised studies are ongoing and there is much interest in trials in other areas of AML.

Thus the current guidelines for the treatment of AML will have to incorporate the new approved drugs but there is a need in every case for further prospective trials to fully explode the potential of these drugs. In addition to these 8 new drugs several new drugs will emerge for similar evaluation.

SP-08

Molecular monitorization of CML under TKI therapy

Guray Saydam

Department of Hematology, Ege University Hospital, Izmir, Turkey

Chronic myeloid leukemia (CML) is a disease, which is characterized by presence of Philadelphia chromosome in almost all cases. This chromosome is detected as reciprocal translocation of chromosome 9 and 22 which results in occurrence of mRNA transcript so called bcrabl. Treatment of CML has evolved in last two decade as introduction of imatinib as a first TKI into the precise medical treatment of CML. Before that, interferons and allogeneic stem have been widely used for treatment of patients with CML. However,

monitorization and follow up of treatment has been always difficult due to some obstacles.

After establishment of TKIs as a golden standard of therapy for CML, some new definitions have been created such as complete hematological response (CHR), complete cytogenetical response (CCyR) and complete molecular response (CMR) or major molecular response (MMR). Those terms have been widely used in monitorization of not only the disease, but also the success of TKI therapy. At the beginning of TKI therapy era, CCyR seemed to be the most reliable surrogate marker for obtaining long PFS and long OS if possible, due to some technical reasons and difficulties, it could not be applied into each and every steps of therapy monitorization.

After IRIS trial, and after many other studies, International Scale (IS) of bcrabl has been accepted as reliable and widely accepted follow-up method for molecular monitorization of CML.

By the efforts of ELN and NCCN, certain time points for molecular monitorization of patients with CML treated with TKI such as 3,6,9, and 12th months as an important decision-making spot. The terminology of CMR/MMR has been replaced with molecular response (MR) with the numbers like 4 or 5 indicating the deepness of response. MMR represents MR3.

Many large cohorts in clinical trials including Dasision and Enestnd showed the importance of having early molecular response in patients with CML and treated with TKIs. Patients with bcrabl level less or equal to 10% at 3rd month of TKI therapy would have less progression rates and long DFS rates compared to those with bcrabl level more than10%.

The earlier and deeper molecular response can be emphasized as the longer PFS and lower progression rates with any TKI.

The earlier and deeper molecular response is also prerequisite of treatment-free remission efforts.

In this presentation, the abovementioned points will be discussed in details.

SP-09

Generic TKI: do they change the strategy of CML therapy*?*

Tomasz Sacha
Jagiellonian University Hospital, Krakow, Poland

Imatinib shortly after introduction has become a first- choice therapy in patients with CML allowing substantial proportion of patients to achieve not only complete cytogenetic response (CCyR) but also deep molecular response (DMR). In the International Randomized Study of Interferon vs STI571 (imatinib) (the IRIS trial), in the German CML-IV study as well as in other independent retrospective studies it was demonstrated that patients who achieve and maintain CCyR for at least two years have the life expectancy approaching that of the general population. Response to TKI therapy is assessed by hematologic, cytogenetic, and molecular testing and the results should be analysed in the pre-defined time points and interpreted in the context of treatment recommendations established by the European Leukemia Net (ELN) panel experts and members of the National Comprehensive Cancer Network (NCCN). Patients without optimal response to TKI according to international recommendations have an increased risk of relapse, of progression and of death related to CML. The achievement of CCyR is associated with the highest probability of long-term survival for CML patients, therefore it could be considered still as an important goal of therapy. However, in a 4-year landmark analysis of the German CML-study IV it was shown that the achievement of a stable MR4.5 is associated with a statistically significant better survival at 8 years with respect to those patients who have achieved CCyR without MMR. Using more potent second-generation TKIs (2GTKI) patients are more likely to achieve faster and deeper molecular response than with imatinib, however the clinical benefit of achieving more rapid responses is undetermined. Nevertheless, sustained deep molecular response (MR4, MR4.5 or MR5) could be a treatment goal for many patients, since proportion of them with time, might be able to safely discontinue TKIs and remain in durable treatment-free remission (TFR). It should be noted that long-term use of 2GTKIs has been associated with potentially serious adverse events such as metabolic disturbances leading to atherosclerosis induction, cardiovascular events or pleural effusion and which may increase disease morbidity or mortality. The life expectancy of patients with CML who achieve optimal responses to TKIs is approaching that of healthy individuals, therefore the prevalence of CML and the cost of TKI therapy is steadily increasing. The high cost of imatinib and 2GTKI therapy is an important concern for healthcare payers especially in countries with restricted resources. Generic imatinib is already available in several countries since couple of years. In Poland the reimbursement of branded imatinib was stopped on 1st July 2014 as in first European country, and imatinib generics entered the market. At the moment of generic introduction several and serious concerns regarding their efficacy and safety have been raised, causing anxiety among many patients in Poland. To provide clinical data on efficacy and safety in a large cohort of patients, who started CML therapy with the use of imatinib generic at the diagnosis or were switched to generic from branded imatinib the Polish Adult Leukemia Group (PALG) Imatinib Generics Registry was established in 2014. The results after three years of observation indicate that molecular and cytogenetic response rates and side-effect rates on imatinib generics and branded imatinib are alike when used in the upfront setting, as well as when used subsequently. The analysis of patients in the intention-to-treat population of the IRIS trial indicated, that after 10 years of follow-up the percentage of patients achieving DMR accounts for 23.3%, and 21,6% after 6 years of imatinib treatment within another study. Approximately 50% of those who achieve DMR and fulfil the criteria for imatinib discontinuation could achieve long-lasting treatment-free remission (TFR) as demonstrated by many discontinuation trials. The chance for durable TFR have therefore about 10% of patients treated initially and continuously with imatinib or imatinib generic. Patients treated with 2GTKIs upfront have a better chance to achieve early molecular response (reduction of BCR-ABL1 transcript to ≤10% at 3 months) than receiving imatinib. The Evaluating Nilotinib Efficacy and Safety in Clinical Trials–Newly Diagnosed Patients (ENESTnd) study comparing first-line nilotinib with imatinib showed that 55% of patients who received nilotinib achieved MR4.5 by 6 years, compared with 45% who received imatinib. The ENESTnd and ENESTfreedom trials have shown that the rates of patients who met the criteria for attempting TFR during therapy with Nilotinib 300 mg BID, Nilotinib 400 mg BID were almost doubled when compared to Imatinib 400 mg QD (37.9%, 34.2% and 21.6%, respectively). It should be emphasized however that the long-term use of 2GTKI has been associated with adverse events such as higher rate of cardiovascular and cerebrovascular events, and it should raise concerns for its use, particularly in some categories of patients. The comorbidities (such as atherosclerosis and its complications, disorders in lipid and glucose metabolism, congestive heart failure, hypertension, etc.) appear in group of CML patients with increasing with age and with prolongation of TKI therapy incidences. The strategy of CML therapy should be based on early identification of patients requiring more intense therapy. Recently developed Eutos Long-Term Survival Score (ELTS) could better discriminate groups of patients with a different chance to achieve major molecular response, MR4.0. and leukemia-free survival in the age category of >65 years. In the Italian observational study 1051 patients newly diagnosed with CML were treated initially with imatinib (n=510; 48.5%) and with 2GTKI (n=541; 51.4%). The rate of DMR achieved with 2GTKI were higher at months 3, 6and 12 than with imatinib. Additionally, in the intermediate ELTS risk group administration of 2GTKI was associated with significantly better 4-year OS when compared to imatinib (99% vs 90,5%; p=0.0030). ELTS could be therefore recommended to assess the baseline disease-risk in this group of patients and to select candidates for frontline therapy with 2GTKI and minimizing the risk for overtreatment. The prognostic significance of early decline of BCR-ABL1 transcript level have been suggested in many studies. The strongest predictor for OS, progression- free survival (PFS) or event-free survival (EFS), but also for the chance to achieve DMR which could open the possibility of discontinuation trial is the early molecular and cytogenetic response. The faster and deeper molecular responses achieved with 2GTKIs may increase the number of patients eligible for TFR, however the choice of TKI therapy should take into account the safety and tolerability of drug of choice and last but not least patient characteristics, particularly age and comorbidities. For successful TFR patients must be willing and able to comply with the requirement for frequent monitoring, which should be sensitive, adequate, rapid, and performed in certified laboratories issuing the results of Real-Time Quantitative PCR (RQ-PCR) using the international scale

(IS). This is essential for safety of the new CML therapy strategy which lead to TKI discontinuation in increasing number of patients.

SP-10
Experience of thalassemia center

Valeh Huseynov
Thalassemia Center, Educational-Therapeutic Clinic of Azerbaijan Medical University, Baku, Azerbaijan

More than 5% of the Azerbaijani population are carriers of thalassemia and there are thousands of people who suffer from it. The Thalassemia Center has been operating in our country for more than 10 years to combat this problem. The main purpose of the establishment of the center is the establishment of specialized medical institutions and blood banks, training of highly qualified personnel, provision of safe and quality blood components to children suffering from thalassemia, as well as medical services. The Thalassemia Center provides extensive opportunities for examination and treatment not only of patients with thalassemia, but also of our patients suffering from oncohematological and other diseases.
The Thalassemia Center has a 30-bed Hematology Department since July 17, 2011. Here the treatment and treatment of children under the age of 18 years and patients of various profile is carried out successfully. Treatment is mainly based on ALL-MB 2015, ALL REZ BFM 2002, BFM, FLAG, FLAG-IDA, EMA protocols.
For most children with HLA-eligible Beta thalassemia, STI treatment is considered the only chance to return to normalcy. Since 2013, the Bone Marrow Transplantation Unit has been operating in the Thalassemia Center. In May 2014-July 2019, 61 and a total of 77 allogenic bone marrow transplants were diagnosed with Beta Thalassemia at the Thalassemia Center. The mortality rate for patients diagnosed with Beta Thalassemia is 96.7%, 83.6%, and 3.27%, respectively, with no survivorship and tearing. There have been no reported fatalities due to hemorrhage. The vast majority of patients are classified as Pesaro Class 2 and Pesaro Class 3 with 47.5% 14.7%. There is no significant difference between Pesaro grades for transplant risk (class1: 4%, class2: 6%, class 3: –4%).
The myeloablature regimens are based on busulfan (Bu) and cyclophosphamide (Cy) protocols. Since 2016, the frequency of transpalant depletion decreased after protocol modifications (addition of Ttheothepa (Th) and/or fludarabine (Flu)).
Transplant host response (TSQR) graphite versus host disease (GVHD) was seen as acute GVHD in 20% of cases and chronic (cronic GVHD) in 2% of cases. The center also had 10 acute leukemia, 5 aplastic anemia, 1 allelogenic and 2 non-Hodgkin lymphoma diagnosis with myelodysplastic syndrome diagnosis.

SP-11
Transfusion support of patients following HSCT

Claudia S. Cohn
The University of Minnesota, Minneapolis, MN, USA

Transfusion support for HSCT patients must include consideration of the patient blood type, donor blood type(s), and the chemotherapy regimen used. Providing compatible components depends on the patient and donor types as well as the engraftment status of the patient. Common complications such as passenger lymphocyte syndrome and pure red cell aplasia should be considered when patients have increased or prolonged red cell requirements. Basic steps can be taken for some patients to prevent some of these complications

SP-13
New hemostatic agents in bleeding and coagulation abnormalities

Jose A. Cancelas
University of Cincinnati College of Medicine, Cincinnati, USA

Platelet transfusion is a widely used therapy in treating or preventing bleeding and hemorrhage in patients with thrombocytopenia or trauma. Compared to the relative ease of platelet transfusion, current practice for platelet storage at room temperature for up to 5–7 days is inefficient, costly, wasteful and relatively unsafe. This presentation will focus on the major advances in platelet derivative products with improved hemostatic potential and safety feature. Recent progress in understanding the platelet activation and host clearance mechanisms has led to reassessments of current and new storage conditions that employ refrigeration and/or cryopreservation to overcome storage lesions and significantly extend shelf life of platelets with reduced risk of pathogen contamination. It is anticipated that future platelet preservation involving cold, frozen and/or pathogen reduction strategies in proper platelet additive solutions will enable longer term and safer platelet storage.

SP-12
How I treat relapsed/refractory DLBCL patients

Carmino De Souza
University of Campinas – UNICAMP, SP, Brazil

The first aspect refers to the histological type. Aggressive lymphomas constitute a large heterogeneous group with two subgroups defined by immunophenotyping (B or T). The most frequent and most involved in the studies is the DLBCL. The immunophenotypic T carries a worse prognosis in the international studies. The IPI (international prognostic index) and the lymphoma signature obtained by microarray are two important markers in this definition. Specifically, IPI has been widely used and its usefulness confirmed in various realities. The role of PET-CT as a modern and responsive marker of response is highlighted and, even in early evaluations such as after the second cycle of chemotherapy, is capable of having a relevant prognostic value. Studies of the GELA group show the prognostic value of the use of PET/CT in terms of PFS (progression free survival). The GELA studies in DLBCL with ASCT in patients <60 years and with 2–3 adverse factors in IPI with the intensified protocol ACVBP (NHL98-3B) versus ACVBP plus Rituximab (NHL03-3B) in historical comparison shows an advantage in terms of overall response and relapse reduction for the Rituximab protocol. Other studies of the same group using Rituximab before and after ASCT also confirmed their usefulness, regardless of the conditioning regimen used to ASCT. Other experiments such as the Italian group with using high-dose sequential therapy plus ASCT and the German group using the Mega-CHOEP protocol, always associated with Rituximab presented more favorable evolutions with the monoclonal antibody even in this group of unfavorable prognosis. The NHL07-3B study compiled this prior knowledge and analyzed the persistence of PET/CT positivity after a few cycles (2) of conventional chemotherapy (R-CHOP14) versus intensified (R-ACVBP14) and conditioning with immunochemotherapy. In this new era, countless studies are in progress and many have as goal to confirm these findings, which are fundamental to future therapeutic. German studies tested chemotherapy in stepwise dose plus a second ASCT and dose-dense chemotherapy plus dose-dense Rituximab; An Italian study used high dose chemotherapy supplemented with Rituximab + ASCT; and finally the French group tested intensified chemotherapy with Rituximab guided by PET/CT. All of these studies confirm the utility of Rituximab inclusion as part of salvage treatment that includes high dose therapy associated with ASCT. Another aspect of extreme relevance concerns to relapsed and/or refractory DLBCL patients with poor prognosis is how to improve their survival in the Rituximab era. Several randomized trials, beginning with the PARMA study, showed the ASCT was the best salvage therapy before Rituximab period, despite of not having confirmed its real importance as first-line therapy in randomized studies and in the meta-analysis with more than 2000 patients, even in pts with poor prognosis. The Hovon-44 study showed in a randomized study that the addition of Rituximab to the classic DHAP protocol followed by ASCT, promoted a statistically significant improvement in terms of overall survival and FFS. The CORAL trial comparing 3 cycles of R-ICE versus 3 cycles of R-DHAP followed by ASCT in chemosensitive patients followed by six months of Rituximab as maintenance versus observation only demonstrated statistically significant advantages in terms of overall survival and event-free survival for patients who used Rituximab as maintenance. Finally, the combination of chemotherapy with Rituximab produced high response rates (82%) and 66% of EFS in two years, when applied in relapsed pts who did not

use Rituximab previously; whereas in refractory patients (relapses with less than one year) these percentages were 54% and 34%, respectively. After ASCT, patients who used Rituximab had only 17% negative events with low toxicity rates.

Salvage treatment for relapsed and/or refractory aggressive non-Hodgkin's lymphoma (specifically DLBCL)

Aggressive NHL relapses, after initial therapy, have a poor prognosis and additional chemotherapy, rarely induce the second long-term remission [1]. Relapses occur in about 40% of cases. Salvage therapy with cytostatic agents, not used in the first line, was introduced in an attempt to rescue these pts [2]. Salvage schemes such as DHAP [3]; ESHAP [4]; ICE [5], result in complete remission (CR) rates ranging from 10 to 37% and 2-year overall survival (OS) less than 25%. Phase 2 studies have demonstrated benefits in chemosensitive patients prior to transplantation [6]. In our experience, 2- and 5-year OS ranged from 60% to 30%; disease-free survival rates (DFS) was 51% to 37% and event-free survival (EFS) 48% to 36% [7]. In these studies, mortality related to transplant (MRT) were from 2.5% to 12%, and relapse post-transplant ranged 35% to 57%. The Parma [8] study demonstrated definitively the superiority of ASCT (autologous stem cell transplantation) in NHL patients, with a chemosensitive relapse when compared to the salvage DHAP protocol. The OS was 53% for ASCT and 32% for DHAP ($p=0.038$); whereas EFS was 46% and 12% ($p=0.001$), respectively. BLAY et al analyzed in this study the importance of IPI in the results [9]. In low-risk IPI patients, there was no difference between therapeutic arms. In patients with one or more IPI prognostic factors, there was a significant difference in progression-free survival (PFS) with better results for the ASCT arm ($p<0.0001$). In 1999, an international jury established ASCT as a treatment of choice for sensitive relapses in NHL [10]. In a study of Brazilian oncohematology study group (GEMOH), published in 2002, the high dose sequence of cyclophosphamide, etoposide and ASCT as salvage therapy in relapsed NHL was analyzed and reported the importance of chemosensitive relapse previous to ASCT. The OS in chemosensitive patients was 92% versus 0% in resistant patients ($p<0.0005$), all resistant patients died within 200 days after ASCT. The IPI at the relapse moment in these patients can predict the ASCT outcomes performed in second or partial remission. Lerner et al. [11] found in high risk IPI patients, a two-fold higher risk of mortality and relapse after ASCT when compared to low-risk IPI pts. Independent prognostic factors for OS and PFS were high-risk IPI and bone marrow involvement at diagnosis. Besides that, they concluded the high risk IPI patients should be considered for different therapeutic modalities. Thus, the well-established role of ASCT in relapse lymphomas suggested the possibility of incorporating ASCT as part of the first-line therapy. Phase II studies showed that the use of this strategy could be superior to conventional CT, producing long remissions in 70 to 80% of patients [12–14]. In high-risk IPI (IPI 2-3) patients the results suggested that HDT followed by ASCT could cure 50% of these pts [15].

References

[1] Rosemberg AS. Autologous bone marrow transplantation in non-Hodgkin's lymphoma. N Engl J Med 1987;316:1541–42.
[2] Gisselbrecht C. Autologous stem cell transplantation in aggressive non-Hodgkins lymphoma. Hematol Cell Ther 1996;38:297–304.
[3] Velasquez WS, Cabanillas F, Salvador P, et al. Effective salvage therapy for lymphoma with cisplatin in combination with high-dose Ara-C and dexamethasone (DHAP). Blood 1988;71:117–22.
[4] Velasquez WS, Mclaughlin P, Tucker S, et al. ESHAP – an effective chemotherapy regimen in refractory and relapsing lymphoma: a 4-year follow-up study. J Clin Oncol 1994;12:1169–76.
[5] Abali H, Urun Y, OKsuzoglu et al. Comparison of ICE (ifosfamide-carboplatin-etoposide) versus DHAP (cytosine arabinosideo-cisplatin-dexamethasone) as salvage chemotherapy in patients with relapsed or refractory lymphoma. Cancer Invest 2008;26:401–6.
[6] Surbone A, Armitage JO, Gale RP. Autotransplantation in lymphoma: better therapy or healthier patients? Ann Intern Med 1991;114:1059–60.
[7] Baldissera RC, Aranha JFP, Oliveira G et al. High-dose cyclophosphamide followed by autologous peripheral blood transplantation improves the salvage treatment for persistent or sensitive relapsed malignant lymphoma. Braz J Med Biol Res 2002;35:49–57.
[8] Philip T, Guglielmi C, Hagenbeek A, et al. Autologous bone marrow transplantation as compared with salvage chemotherapy in relapses of chemotherapy-sensitive non-Hodgkin's lymphoma. N Engl J Med 1995;333:1540–5.
[9] Blay JY, Gomez F, Sebban F, et al. The International Prognosis Index correlates to survival in patients with aggressive lymphoma in relapse: analysis of the PARMA trial. Blood 1998;10:3562–68.
[10] Shipp MA, Abeloff KH, Antman G, et al. International consensus conference on high-dose therapy with hematopoietic stem cell transplantation in aggressive non-Hodgkin's lymphomas: report of the jury. J Clin Oncol 1999;17:423:29.
[11] Lerner RE, Thomas W, Defor TE, et al. The International Prognostic Index assessed at relapse predicts outcomes of autologous transplantation for diffuse large-cell non-Hodgkin lymphoma in second complete or partial remission. Biol Blood Marrow Transplant 2007;13:486–92.
[12] Weaver Ch, Schwartzberg L, Zhen B, et al. High-dose chemotherapy and peripheral blood stem cell infusion in patients with non-Hodgkin's lymphoma: results of outpatient treatment in community cancer centers. Bone Marrow Transplant 1997;20:753–60.
[13] Bolwell B, Goormastic M, Andresen S, et al. Durability of remission after ABMT for NHL: the importance of the 2-year evaluation point. Bone Marrow Transplant 1997;19:443–48.
[14] Vitolo U, Cortelazzo S, Liberati AM, et al. Intensified and high-dose chemotherapy with granulocyte colony-stimulating factor and autologous stem-cell transplantation support as first-line therapy in high-risk diffuse large-cell lymphoma. J Clin Oncol 1997;15:491–498.
[15] Cortelazzo S, Rossi A, Viero P, et al. BEAM chemotherapy and autologous haematopoietic progenitor cell transplantation as front-line therapy for high-risk patients with diffuse large cell lymphoma. Br J Haematol 1999;99 (2):379–85.

SP-14

Risk stratification and treatment of chronic lymphocytic leukemia (CLL)

Robin Foà
Hematology, Department of Translational and Precision Medicine, "Sapienza" University, Rome, Italy

CLL is the most frequent leukemia in the Western hemisphere, while it is rare in other geographic areas. The median age at presentation is around 70 years. For an optimal diagnostic-prognostic management, a broad and integrated morphologic, immunophenotypic, cytogenetic and molecular work-up is today mandatory. This in first place enables a precise differential diagnosis between CLL and other lymphoproliferative disorders, including non-Hodgkin's lymphomas in leukemic phase. Once a correct diagnosis of CLL is made, it is possible to identify parameters associated with a different prognostic likelihood. A broad number of biologically based prognostic markers have been identified. At present, the only biologic parameters that effectively can guide treatment, outside of clinical trials, is the presence of a 17p deletion and/or TP53 mutation. These abnormalities are associated with an unfavorable prognosis and should be investigated at the time of each line of treatment, as they can be acquired over time. 11q deletion should also be investigated, as well as the IGHV mutational status. The latter remains unmodified during the course of the disease and is very helpful in terms of deciding how to treat patients.

Chemotherapy, usually associated with an anti-CD20 monoclonal antibody, has been the treatment of choice for decades. The scenario has changed following the advent of mechanism-based drugs. The first approved drugs have been agents capable of targeting pathways downstream of the B-cell receptor (BCR): ibrutinib, a Bruton tyrosine kinase inhibitor, and idelalisib, a PI3 kinase delta inhibitor. Ibrutinib and idelalisib (with rituximab) were initially approved by EMA for the treatment of relapsed/refractory (R/R) CLL patients and front-line for patients with 17p deletion/TP53 mutation. More recently, FDA and EMA have approved the use of ibrutinib front-line for all CLL patients. Great interest has been generated by the results obtained with the Bcl-2 inhibitor venetoclax, which has a much more profound debulking activity compared to the BCR antagonists. The results obtained have led to the

approval of venetoclax for the treatment of CLL patients following at least one prior therapy. More recently, veneteclox in combination with rituximab has also been approved for R/R CLL.

With chemoimmunotherapy, a proportion of patients with a favorable biologic profile may obtain a status of minimal residual disease (MRD) negativity and be potentially cured. Ongoing studies are documenting the profound anti-leukemic activity of the combination of new (and old) drugs. This is associated with a high number of patients becoming MRD- in the blood and marrow. If confirmed and associated with a good safety profile, this combined approach may further change our strategy in CLL management, opening an era of potential disease eradication/cure and treatment discontinuation. This clearly would further broaden the issues of accessibility (to drugs and technologies) and sustainability.

SP-15

Molecular markers in chronic lymphocytic leukemia (CLL)

P. Panayiotidis

Prof of Haematology, National and Kapodistrian University of Athens(NKUA), Head, Unit of Molecular Diagnostic in Haematology, NKUA, Athens, Greece

CLL is an indolent neoplastic disease of monoclonal B lymphocytes. Diagnosis of CLL is done with morphology and immunophenotype by FACS analysis with a panel of specified monoclonal antibodies.

Molecular analysis is not useful for the diagnosis of CLL, but is needed for:

1) at diagnosis, in order to define if a CLL patient has mutated or un-mutated monoclonal IgVH sequence, in the monoclonal neoplastic CLL lymphocytes. Analysis of the IGVH DNA sequence with specific search tools, identifies two subgroups in CLL:
   a) "Mutated" Pts, with the presence of > 2% mutations (hypermutated monoclonal IgVH DNA sequence), with good clinical prognosis),
   b) "Unmutated" Pts with <2% mutations in the monoclonal IgVH DNA sequence, and worse clinical prognosis.

In around 30% of patients with CLL, their IgVH sequence, belongs to different "stereotype" subsets, that have different prognosis, to the one predicted by the mutational status (unmutated vs mutated IgVH sequence).

The IgVH DNA sequence remains the same during the course of the disease in a CLL patient, and there is no need to repeat this test at different time points in a CLL patient.

2) Before initiation of treatment in a CLL patient, these tests should be done, according to IWCLL guidelines:
   a) del of p53 by FISH analysis.
   b) mutations in the p53 gene by DNA sequence
   c) In parallel, karyotypic analysis of in vitro stimulated CLL cells can be done and this has prognostic value.

It is clear that p53 analysis (FISH and mutations) should be repeated before any line of treatment in a CLL patient, since results are different during the course of the disease and type of therapies used.

ERIC (European Research Initiative in CLL) has organized successfully the certification of different labs in Europe and abroad in the analysis of IgVH and P53 mutations.

These molecular tests can quide the selection of the best possible therapy for every individual CLL patient. Although recommended as companion diagnostics by all CLL guidelines, in very few countries the cost of these tests is covered by their National Health system.

This creates a paradox, where very expensive drugs are approved and used for the therapy of CLL, but the cost of the necessary companion molecular diagnostic tests, needed for the proper selection of therapy, is not covered!

SP-16

New drugs for CLL

Antonio Cuneo

Hematology Unit, University of Ferrara

Treatment of chronic lymphocytic leukemia (CLL) has dramatically changed over the last years thanks to basic research advances and a number of well conducted clinical trials. The introduction of mechanism-based drugs, their combination with anti-CD20 monoclonal antibodies (mAb) or with chemoimmunotherapy (CIT), and the development of novel agents with greater selectivity represents a major advance in first line and in relapsed/refractory (R/R) setting.

Ibrutinib

Results of the RESONATE-2 trial supported approval of ibrutinib for first-line treatment of CLL. 269 patients aged ≥65 years (median age 73 on ibrutinib arm, 72 on chlorambucil arm) with previously untreated CLL without del(17p) were randomized to ibrutinib until disease progression or unacceptable toxicity (n=136) or chlorambucil (n=133) for 12 cycles. Patients between the ages of 65 and 70 years had a comorbidity precluding FCR. In the ibrutinib arm 48% had U-IGHV. The primary analysis [1] with a median follow up of 18.4 months demonstrated superiority of ibrutinib vs chlorambucil for PFS (median not reached vs 18.9 months), OS (median not reached in both arms) and ORR (86% vs 35%). At the time of the primary analysis 20 patients had died (3 and 17 on ibrutinib and chlorambucil, respectively) and 33 of 133 patients randomized to chlorambucil had crossed over to receive ibrutinib (extension study) after progressive disease (PD) [2]. The objective of the supplemental analysis was to assess OS with longer follow up and adjusted for crossover. This supplemental OS analysis demonstrated a statistically significant survival benefit for single-agent ibrutinib over chlorambucil in older patients with treatment-naïve (TN) CLL. In the extended analysis of RESONATE-2 [3] 107 patients (79%) remain on ibrutinib (median follow-up of 29 months). CR increased substantially from 7% at 12 months to 18% with extended follow-up, with an ORR of 92%. Ibrutinib significantly prolonged PFS vs chlorambucil (median not reached vs 15 months). No significant PFS difference was observed in the ibrutinib arm in patients with unmutated (U) vs mutated (M) IGHV (24-month PFS 90% and 89%, respectively). PFS at 24 months were also similar regardless of age (<75 years [88%], ≥75 years [89%]). Likewise, OS was similar regardless of age (OS <75 years [94%], ≥75 years [96%]). With longer follow-up and despite crossover, ibrutinib continues to demonstrate an OS benefit compared with chlorambucil with a 24-month OS of 95% for ibrutinib vs 84% for chlorambucil.

Importantly a survival advantage was documented in the E1912 trial coordinated by the Eastern Cooperative Oncology Group–American College of Radiology Imaging Network. In this independent study fit patients (≤70 years of age) without 17p deletion were radomized in a 2:1 ratio to receiving ibrutinib and rituximab for six cycles followed by ibrutinib until disease progression, or 6 cycles of chemoimmunotherapy with FCR [4]. At a median follow-up of 33.6 months, 4 deaths were recorded among 354 patients in the ibrutinib arm as compared with 10 deaths among 175 patients in the FCR arm (hazard ratio 0.17; 95% CI, 0.05 to 0.54; P<0.001). A PFS advantage was noted in the ibrutinib arm in CLL with IGHV unmutated, whereas no PFS difference was noted in CLL patients with IGHV mutated. LIkewise, a loinger PFS was observed in the ibrutinib arms in 2 trials comparing ibrutinib with bendamustine and rituximab or chlorambucil and obinutuzumab [5,6]. However, in the latter two trials no survival difference was reported between patients treated in the ibrutinib arms or in the CIT arms.

The phase 3 RESONATE trial compared single-agent ibrutinib to ofatumumab in 391 patients with relapsed/refractory CLL (ibrutinib n=195, ofatumumab n=196) with a median age of 67 (≥70 40% and 41% in the two group respectively) [7]. A large proportion of patients had high risk features, including del(17p) (32% in ibrutinib arm; 33% in ofatumumab arm) or *TP53* mutation (51% and 46%, respectively). The primary analysis at a median follow up of 9.7 months demonstrated superiority of ibrutinib over ofatumumab in terms of PFS, OS and ORR. The superiority of ibrutinib was maintained with median follow-up of 44 months without unexpected long-term safety signals. Investigators also observed durable remissions among patients of all genomic groups, including those with del(17p), del(11q) or U-IGHV. Coutre et al. [8] conducted an integrated safety analysis of single-agent ibrutinib from the RESONATE and RESONATE-2 trials (ibrutinib up to 43 months), and examined longer-term safety separately in the phase 1b/2 PCYC-1102/1103 study (exposure to ibrutinib up to 67 months). The most common grade 3–4 AEs were neutropenia and pneumonia. The most common AEs contributing to discontinuation were pneumonia (n=4), anemia (n=3) and atrial fibrillation

(n=3). With long-term follow-up on PCYC-1102/1103 AEs were similar to those in the integrated analysis.

Idelalisib

A randomized, double-blind, phase III trial of idelalisib (Idela) plus rituximab vs placebo plus rituximab in patients with relapsed CLL was terminated early because of superior efficacy of Idela-plus-rituximab (Idela/R) arm [9]. The median age was 71 years. 78% of patients were ≥65 years of age; 40% had at least moderate renal dysfunction (creatinine clearance <60 ml/min) and 85% had CIRS score >6. Patients had received a median of three prior lines of therapy. Either del(17p) or *TP53* mutation was present at screening in 43.2% of patients and 83.6% of patients had U-IGHV. Patient characteristics were balanced across treatment arms. Patients in the Idela arm received the study drug until progression or unacceptable toxicity and patients in the rituximab plus placebo arm crossed over to idelalisib at progression (extension study). Sharman et al. [10] reported the long-term efficacy and safety across the primary and extension study. Overall 161 patients transitioned from the primary study to the extension study (n=75 patients from the Idela/R arm and n=86 from the placebo/R arm). As of August 2018, no patients remained in the extension study (106 patients died; 50 in the Idela/R arm and 56 in the placebo/R arm). Main causes of death were advanced CLL and the underlying frailty, poor prognosis and AEs. The ORR for patients in the Idela/R-to-Idela arm was 85.5% with one CR (0,9%). The median duration of response was 21.4 months. The Idela/R-to-Idela group had a median PFS of 20.3 months after a median follow-up time of 18 months. The median PFS was 20.8 months in patients with neither del(17p) nor *TP53* mutation and was 18.7 months in patients with either del(17p) or *TP53* mutation. The median PFS was 22.1 months vs 19.4 months in patients with M-IGHV vs U-IGHV. The median OS was 40.6 months and 34.6 months for patients randomly assigned to the Idela/R and placebo/R groups, respectively. Treatment with Idela/R significantly prolonged survival in patients with either del(17p) or *TP53* mutations compared with those treated with placebo/R. No new IDELA-related adverse events were identified with longer exposure.

Venetoclax

Following the demonstration of its activity as single agent [11] venetoclax was combined with rituximab in a phase 1b study [12], showing acceptable safety. These data prompted investigators to design trials combining venetoclax and anti CD20 monoclonal antibodies.

The CLL14 trial [13] is a randomized open-label, phase 3 trial which investigated fixed-duration treatment with venetoclax–obinutuzumab in 432 patients (216 assigned to each group) with previously untreated CLL and coexisting conditions. The characteristics were well balanced between the two groups. Median age was 72 years; median CIRS score was 8. Median creatinine clearance was 66.4 ml/min; 59.8% had U-IGHV. 13.8% of patients had *TP53* deletion, mutation, or both. The percentage of patients attaining CR and minimal residual disease (MRD) negativity in peripheral blood (PB) or bone marrow (BM) were higher with venetoclax–obinutuzumab than with chlorambucil–obinutuzumab (PB 42.1% vs. 14.4%; BM 33.8% vs. 10.6%). Venetoclax–obinutuzumab was superior to chlorambucil–obinutuzumab in all the prognostic subgroups. The ORR was 84.7% vs 71.3%; CR 49.5% vs 23.1%; estimated 24 months-PFS was 88.2% in the venetoclax–obinutuzumab group as compared with 64.1% in the chlorambucil–obinutuzumab group. This benefit was also observed in patients without *TP53* deletion or mutation. A longer PFS was reported in patients with U-IGHV patients, whereas no PFS difference was observed in the two treatment arms in patients with mutated IGHV. Median OS was not reached in either group.

In the phase 1b study by Seymour et al. [12], 49 R/R CLL patients were treated with Venetoclax–Rituximab (VR). This combination attained an 86% ORR, including 51% CR/CRi, leading to a 2-year PFS of 82% and a 57% BM MRD-negativity rate. 13 responders elected to discontinue Venetoclax and 8 who were MRD negative remain in ongoing remission after a median of 9.7 months off Venetoclax.

In the randomized, open-label, phase 3 MURANO trial, Seymour et al. [14] evaluated the efficacy of VR in R/R CLL. 389 patients (age≥18 years; median age 65) were randomly assigned to receive venetoclax for up to 2 years plus rituximab for the first 6 months (VR group) or bendamustine plus rituximab for 6 months (BR group). The characteristics of the groups were balanced. Patients had received 1–3 previous treatments. ECOG performance status was 0 or 1 with adequate hepatic and renal function. 246 of 360 patients had U-IGHV. 92 of 342 (26.9%) patients who were assessed for chromosome 17p status had a del(17p), 99 of 376 (26.3%) patients who were tested for *TP53* had *TP53* mutations. Median follow-up was 23.8 months. ORR was 92.3% in VR group and 72.3% in BR group.

MRD disease in PB samples taken at month 9 was detected in 62.4% and 13.3% of the patients in the VR and BR group, respectively.

PFS was significantly higher in the VR group (32 PD or death in 194 patients) than in the BR group (114 events in 195 patients); the 2-year PFS was 84.9% and 36.3%, respectively. The benefit was maintained across all subgroups. The 2-year PFS among patients with del(17p) was 81.5% in VR group vs 27.8% in BR group and the 2-year PFS among those without del(17p) was 85.9% vs 41.0%. OS also showed meaningful benefit with VR. The 24-month OS was higher in VR group than in BR group (91.9% and 86.6%, respectively).

Acalabrutinib

Acalabrutinib is a potent, covalent BTK inhibitor with greater selectivity and less off-target kinase inhibition compared with ibrutinib in vitro. Awan et al. evaluated the safety and efficacy of acalabrutinib in 33 patients with CLL who discontinued ibrutinib because of intolerance [15]. Median patients age was 64 years (49% ≥65), with ECOG performance status 0–1 in 97% of patients. Patients were heavily pretreated, with a median of 4 prior therapies; 20 patients (61%) had received 4 or more lines of prior therapy. Most patients (81%) had U-IGHV. *TP53* mutation was found in 30% of patients and del(17p) in 38%. After a median of 19.0 months 23/33 patients remained on acalabrutinib whereas 10 had discontinued (PD n=4; AEs n=3). ORR was 76%, including 1 complete, 19 partial responses and 5 partial responses with lymphocytosis. The median duration of response was not reached among 25 responder patients. One-year and 2-year PFS were 83.4% and 75.0%, respectively. In patients with del(11q) (n=7), del(17) (n=12), and U-IGHV (n=25), ORRs were 86%, 67% and 80%, respectively. In patients with 4 or more lines of prior therapies (n=20), ORR was 65% and 2-year PFS 76%. The most frequent AEs were diarrhea, headache, cough. Grade 3/4 AEs occurred in 58% (most commonly neutropenia and thrombocytopenia). Acalabrutinib was well tolerated with a high ORR in patients previously intolerant to ibrutinib.

Results from a pre-planned interim analysis of the ASCEND study were presented at 2019 EHA [16]. This is a randomized, multicenter, open-label phase 3 trial which evaluated efficacy and safety of acalabrutinib monotherapy vs investigator choice therapy (Rituximab plus Idelalisib or Bendamustine) in R/R CLL. Bendamustine plus rituximab (BR) and idelalisib plus rituximab (IdR) are standard therapies for R/R CLL. In this study acalabrutinib was superior to IdR/BR in terms of PFS and the improvement was observed across all subgroups including those with high-risk features. Acalabrutinib had a more tolerable safety profile than IdR/BR.

CIT plus novel agents

Considering that FCR has shown a curative potential for fit and younger CLL patients with M-IGHV, combination regimens with CIT plus novel agents have been designed. A multicentre, open-label, non-randomised, single-arm phase 2 trial of ibrutinib plus FCR (iFCR) for previously untreated younger (≤65 yrs old), fit (adequate organ function, ECOG PS ≤1) patients with CLL was performed [17]. Patients were treated with up to 6 cycles of ibrutinib concurrently with FCR, followed by at least 2 years of ibrutinib maintenance. Patients with a MRD-negative disease in the BM after 2 years of maintenance discontinued ibrutinib. The primary endpoint was the rate of CR with undetectable MRD in the BM 2 months after the last cycle of iFCR. As of the data cutoff of July 2017, 49 pts were accrued, including 35 pts in the original cohort and 14 pts in an expansion cohort. Baseline characteristics included del(17p) in 4/47 tested (9%), U-IGHV in 26/46 tested (57%), *TP53* mutation without del(17p) in 3 pts (6%). The original cohort was not restricted by prognostic marker and included patients with del(17p) or *TP53* aberrations. After a protocol amendment (on March 21, 2017), the protocol enrolled an expansion cohort that included patients without del(17p). At a median follow-up of 16,5 months, CR and undetectable MRD was achieved by 28 (33%) of 85 patients, as compared with a 20% historical value with FCR alone in the CLL8 trial) [18]. One patient had PD and one patient died (sudden cardiac death after 17 months of ibrutinib maintenance). The most common all-grade toxic

effects were haematological. Non-haematological SAEs included grade 3 atrial fibrillation in 4% of patients and grade 3 *Pneumocystis jirovecii* pneumonia (2%). iFCR is promising as a time-limited combination for frontline treatment in younger fit patients. The iFCR study will also provide data on whether U-IGHV patients can achieve durable response with a time-limited regimen.

Obinutuzumab was shown to be superior to rituximab in older adults in the CLL11 trial [19]. In a phase 2 trial [20] ibrutinib was combined with fludarabine, cyclophosphamide and obinutuzumab (iFCG) 32 previously untreated CLL patients with M-IGHV and without *TP53* disruption received this combination. The trial was designed to limit chemotherapy to 3 courses in this genetically favorable subset of CLL, potentially reducing toxicity while maintaining efficacy. The primary endpoint was CR/CRi with undetectable BM MRD after 3 courses of iFCG. Patients who obtained MRD-negativity received Ibrutinib with obinutuzumab (iG) for other 3 cycles, then Ibrutinib for further 6 cycles. Patients not achieving the primary endpoint received iG for 9 cycles. All pts with undetectable MRD at 1 yr stopped therapy. The historical rate of C3 undetectable BM MRD with FCR in IGHV-M pts was 26% [21]. After median follow up of 10,9 months the ORR was 100% and median PFS was not reached. 86% of patients achieved MRD-negative remission in BM at 3 months and 46% achieved CR/CRi with undetectable MRD at 3 months. Responses continued to improve over time (6 months: CR/CRi rate 74%, MRD neg rate 91%; 12 months: CR/CRi rate 75%, MRD neg rate 100%).

Emerging data (HELIOS trial) [22] indicated that the combination of ibrutinib with CIT is safe and effective, even though this approach in unlikely to be adopted in clinical practice because it doesn't appear to offer any advantage over ibrutinib alone.

Combinations of novel agents

Several studies are ongoing that assess the efficacy and safety of combinations of novel agents. One promising combination is ibrutinib plus venetoclax. Venetoclax increases the propensity for CLL cells to undergo apoptosis, and ibrutinib causes CLL cells to become more dependent on bcl-2 for their survival. These complementary effects likely underlie the potent CLL cell-killing that is observed with the combination of these two drugs *ex vivo* [23]. Clinical trials are already underway evaluating this combination. A phase 2 trial of ibrutinib and venetoclax involved previously untreated high-risk and older patients with CLL [24]. Patients had ECOG performance-status 0–2 and creatinine clearance >50 ml/min. All patients had at least one of the following features: del(17p) (18%) mutated *TP53* (14%), del(11q) (25%), U-IGHV (83%) or an age of 65 years or more. Overall, 92% of the patients had U-IGHV, *TP53* aberration, del(11q). Patients received ibrutinib monotherapy for 3 cycles followed by the addition of venetoclax and the drug combination was administered for 24 cycles. A total of 80 patients were treated. Median follow-up was 14.8 months. After 12 cycles of combined treatment, 88% of patients had CR or iCR and 61% had remission with undetectable MRD. Three patients completed 24 cycles of combined therapy; all had CR or iCR with undetectable MRD in BM. Patients ≥65 years had a high rate of response; observed responses were independent of IGHV status, FISH category, *TP53* mutation. The estimated 1-year PFS and OS were 98% and 99% respectively. No patient had CLL progression, 1patient developed Richter's transformation. No unexpected adverse events were recorded. The appropriate duration of treatment with targeted agents remains uncertain and this study and several other ongoing trials are exploring this question.

Rogers et al. [25] conducted a phase-2 study using a 3-drug combination of venetoclax, ibrutinib, and obinutuzumab in 25 previously untreated CLL patients. Median age was 59. Eligible patients had an ECOG PS ≤1 and preserved organ function, including creatinine clearance ≥50 mL/min. Baseline risk characteristics included U-IGHV in 17 (71%) patients and FISH positive for del(17p) in 3 (12%) patients. Treatment was planned for 14 cycles (C) of 28 days each. Response was determined after cycles 8 and 14. The rate of CR, including CRi, was 50% (12/24). MRD-negative status in PB and BM was achieved in 14 (58%) patients. In general, AEs were consistent with the safety profile of the single drugs. Hematologic toxicities were the most frequent high-grade treatment-related AEs. The study is ongoing.

Rogers et al. [26] conducted a phase 1b trial (NCT02427451) of obinutuzumab, ibrutinib and venetoclax in relapsed/refractory CLL patients. The cohort was relatively young with a median age of 57. Patients had a median number of 1 prior treatment and they were required to have a creatinine clearance of ≥50 mL/min. Preliminary data of this phase 1b study demonstrates that this combination therapy is safe and feasible, has a high ORR, and is capable of eliminating MRD. These results justifies future study with this novel triplet combination in cohorts of R/R and TN patients, as well as larger phase 3 trials.

Conclusion

The treatment of CLL is nowadays based on risk-based treatment algorithms. Chemoimmunotherapy still has a role in low-risk patients, whereas new drugs (i.e. ibrutinib or venetoclax) are preferred in high risk patients.

The long-term experience with ibrutinib single agent until progression is very positive and fixed duration treatment with venetoclax and rituximab is a new paradigm for treatment of CLL.

Combination treatment (CIT + ibrutinib or venetoclax combined with ibrutinib) are very promising regimens.

References

[1] Burger JA, Tedeschi A, Barr PM, et al. Ibrutinib as initial therapy for patients with chronic lymphocytic leukemia. N Engl J Med 2015;373(25):2425–37.

[2] Barr PM, Robak T, Owen C, et al. Sustained efficacy and detailed clinical follow-up of first-line ibrutinib treatment in older patients with chronic lymphocytic leukemia: extended phase 3 results from RESONATE-2. Haematologica 2018;103(9):1502–1510.

[3] Barr PM, Robak T, Owen C, et al. Sustained efficacy and detailed clinical follow-up of first-line ibrutinib treatment in older patients with chronic lymphocytic leukemia: extended phase 3 results from RESONATE-2. Haematologica 2018;103(9):1502–1510.

[4] Shanafelt TD, Wang XV, Kay NE, et al. Ibrutinib-rituximab or chemoimmunotherapy for chronic lymphocytic leukemia. N Engl J Med 2019;381(5):432–443.

[5] Woyach JA, Ruppert AS, Heerema NA, et al. Ibrutinib regimens versus chemoimmunotherapy in older patients with untreated CLL. N Engl J Med 2018;379(26):2517–2528.

[6] Moreno C, Greil R, Demirkan F, et al. Ibrutinib plus obinutuzumab versus chlorambucil plus obinutuzumab in first-line treatment of chronic lymphocytic leukaemia (iLLUMINATE): a multicentre, randomised, open-label, phase 3 trial. Lancet Oncol 2019;20(1):43–56.

[7] Byrd JC, Hillmen P, O'Brien S, et al. Long-term follow-up of the RESONATE phase 3 trial of ibrutinib vs ofatumumab. Blood 2019;133(19):2031–2042.

[8] Coutre SE, Byrd JC, Hillmen P, et al. Long-term safety of single-agent ibrutinib in patients with chronic lymphocytic leukemia in 3 pivotal studies. Blood Adv 2019;3(12):1799–1807.

[9] Furman RR, Sharman JP, Coutre SE, et al. Idelalisib and rituximab in relapsed chronic lymphocytic leukemia. N Engl J Med 2014;370(11):997–1007.

[10] Sharman JP, Coutre SE, Furman RR, et al. Final results of a randomized, phase iii study of rituximab with or without idelalisib followed by open-label idelalisib in patients with relapsed chronic lymphocytic leukemia. J Clin Oncol 2019;37(16):1391–1402.

[11] Roberts AW, Davids MS, Pagel JM, et al. Targeting BCL2 with venetoclax in relapsed chronic lymphocytic leukemia. N Engl J Med 2016;374(4):311–22.

[12] Seymour JF, Ma S, Brander DM, et al. Venetoclax plus rituximab in relapsed or refractory chronic lymphocytic leukaemia: a phase 1b study. Lancet Oncol 2017;18(2):230–240.

[13] Fischer K, Al-Sawaf O, Bahlo J, et al. Venetoclax and Obinutuzumab in Patients with CLL and Coexisting Conditions. N Engl J Med 2019;380(23):2225–2236.

[14] Seymour JF, Kipps TJ, Eichhorst B, et al. Venetoclax-Rituximab in Relapsed or Refractory Chronic Lymphocytic Leukemia. N Engl J Med 2018;378(12):1107–1120.

[15] Awan FT, Schuh A, Brown JR, et al. Acalabrutinib monotherapy in patients with chronic lymphocytic leukemia who are intolerant to ibrutinib. Blood Adv 2019;3(9):1553–1562.

[16] Ghia P, Pluta A, Wach M, et al. Ascend phase-3 study of acalabrutinib vs investigators choice of rituximab plus idelalisib (IDR) or bendamustine

(BR) in patients with relapsed/refractory CLL. EHA Library. Jun 16, 2019; 273259; LB2606
[17] Davids MS, Brander DM, Kim HT, et al. Ibrutinib plus fludarabine, cyclophosphamide, and rituximab as initial treatment for younger patients with chronic lymphocytic leukaemia: a single-arm, multicentre, phase 2 trial. Lancet Haematol 2019;6(8):e419–e428.
[18] Hallek M, Fischer K, Fingerle-Rowson G, et al. Addition of rituximab to fludarabine and cyclophosphamide in patients with chronic lymphocytic leukaemia: a randomised, open-label, phase 3 trial. Lancet 2010; 376(9747):1164–74.
[19] Goede V, Fischer K, Busch R, et al. Obinutuzumab plus chlorambucil in patients with CLL and coexisting conditions. N Engl J Med 2014;370(12):1101–10.
[20] Jain N, Thompson PA, Burger JA, et al. Ibrutinib, fludarabine, cyclophosphamide, and obinutuzumab (iFCG) for firstline treatment of patients with CLL with mutated IGHV and without TP53 aberrations. Blood 2018;132:695.
[21] Strati P, Keating MJ, O'Brien SM, et al. Eradication of bone marrow minimal residual disease may prompt early treatment discontinuation in CLL. Blood 2014;123(24):3727–32.
[22] Fraser G, Cramer P, Demirkan F, et al. Updated results from the phase 3 HELIOS study of ibrutinib, bendamustine, and rituximab in relapsed chronic lymphocytic leukemia/small lymphocytic lymphoma. Leukemia 2019;33:969–980.
[23] Cervantes-Gomez F, Lamothe B, Woyach JA, et al. Pharmacological and protein profiling suggests venetoclax (ABT-199) as optimal partner with ibrutinib in chronic lymphocytic leukemia. Clin Cancer Res 2015;21(16):3705–15.
[24] Jain N, Keating M, Thompson P, et al. Ibrutinib and venetoclax for first-line treatment of CLL. N Engl J Med 2019;380(22):2095–2103.
[25] Rogers KA, Huang Y, Stark A, et al. Initial results of the phase 2 treatment naive cohort in a phase 1b/2 study of obinutuzumab, ibrutinib, and venetoclax in chronic lymphocytic leukemia. Blood 2017 130:431.
[26] Rogers KA, Huang Y, Ruppert AS, et al. Phase 1b study of obinutuzumab, ibrutinib, and venetoclax in relapsed and refractory chronic lymphocytic leukemia. Blood 2018;132(15):1568–1572.

SP-18
Update on therapeutic apheresis indications

Joseph Schwartz
College of Physician, Surgeons of Columbia University

The talk will describe the development process and the principles of the Evidence-based Therapeutic Apheresis guidelines published by ASFA every 3 years. It will also highlight the changes made to the most recent edition that was just published in June 2019.

SP-19
Update on extracorporeal photopheresis (ECP)

Jennifer Schneiderman
Ann & Robert H. Lurie Children's Hospital of Chicago

Extracorporeal photopheresis (ECP) was developed in the mid-1980's for the treatment of refractory cutaneous T-cell lymphoma (CTCL); CTCL remains its only Food and Drug Administration approved application. Since that time, several iterations of the device that is used to treat patients have been developed, and its use has been expanded to include other T-cell mediated diseases including GVHD, prevention and treatment of rejection following solid organ transplantation, and selected autoimmune diseases. Several of these applications are evaluated in the most recently published guidelines from the American Society for Apheresis. ECP is an apheresis procedure, which involves the removal of patients' circulating mononuclear cells with an apheresis apparatus, addition of 8-methoxypsoralen (8-MOP), exposure to UV-A light, and return of the treated cells to the patient. Approximately 5–10% of cells circulating in the peripheral blood are treated in each procedure. Many patient variables need to be considered for such treatments, especially in the context of which device is used for cell collection. Such variables include body weight, permissible extracorporeal volume, clinical status at the time of the procedure, potential need for central venous access, along with laboratory values including total white blood cell and platelet counts, hematocrit, and bilirubin. ECP may be performed on a closed system device (predominantly used in the United States) or an off-line procedure where cells are collected with a standard cell separator and treated in the laboratory prior to return to the patient, a procedure more commonly utilized in European centers. Treatment centers utilizing the off-line method have also frozen collected cells in aliquots to be thawed, treated, and re-infused at a later time, without significant differences noted in cell phenotype. This practice allows for patients who travel long distances, those who lack appropriate intravenous access, or cannot tolerate multiple apheresis procedures due to level of illness to receive treatment.

While these differences in treatment practices allow practitioners to treat a wide range of patients in multiple clinical settings, they introduce a considerable number of variables which make globalization of the clinical data available difficult to interpret at times. For example, substantial differences in the numbers of cells collected, treated, and returned to the patient are seen when comparing both US devices and the European method of collection. To date, there have been no organized clinical trials performed to determine if a larger number of treated cells are required for maximal clinical effect. In addition, the basic treatment schedule and subsequent tapering of treatments varies considerably from center to center. Some treating centers will refrain from performing ECP depending on certain patient lab values resulted on the day of treatment, including absolute lymphocyte or monocyte counts. Finally, while the manufacturer advocates for the use of heparin as the principle anticoagulant during the procedure, many centers have adopted the use of citrate either alone or in combination with heparin in patients with higher risk of bleeding. As such, ongoing debate exists as to the optimal way to deliver this therapy to patients. However, despite these limitations, ECP's favorable safety profile and non-immune suppressing mechanism of action make this an attractive therapy for patients.

SP-20
Update on collections for HPC and CAR-T

Anand Padmanabhan
Medical College of Wisconsin

Apheresis-based cellular collections are now the most frequently used technique to collect cellular products to facilitate hematopoietic stem cell transplants and support novel cellular therapies such as CAR-T (Chimeric Antigen Receptor-T cells). This presentation will discuss various aspects related to timing, technique and optimization of cellular collections. The concept of large volume leukapheresis for hematopoietic progenitor cell collections will be discussed as well as strategies to optimize such collections from autologous and allogeneic donors. Specifically, the presenter will detail "prediction" algorithms in place at his institution that assist with "tailoring" stem cell collections. Novel cellular therapies such as CAR-T are increasingly being used for patients with NHL and B-ALL and with additional indications on the horizon, including multiple myeloma. Within the CAR-T context, the speaker will discuss his experience with collection of T lymphocytes and will present collection trends and practices within this nascent field.

SP-21
How I treat multiple myeloma?

Angelo Maiolino
Professor of Medicine, Department of Internal Medicine, Universidade Federal do Rio de Janeiro (UFRJ), Coordinator of Hematology, Americas Centro de Oncologia Integrado, Rio de Janeiro, Brazil

In recent years several new drugs were approved for multiple myeloma (MM) treatment. Three classes are included in almost all lines of MM treatment including the proteasome inhibitors (bortezomib, carfilzomib, and ixazomib) immunomodulators (thalidomide, lenalidomide, and pomalidomide) and monoclonal antibodies (daratumumab and elotuzumab) in different

combinations [1]. Access to these new drugs is essential in the choice of the correct treatment strategy; for example, in my country, Brazil, all these drugs instead pomalidomide were approved, but universal access is still a challenge particularly for patients in the Public Health System (SUS). For first-line treatment, the evaluation of eligibility for autologous stem cell transplant (ASCT) remains mandatory. In addition to age, performance status, and presence of significant comorbidities need to be taken into consideration for eligibility classification [2]. For patients eligible for ASCT, the standard of care initial treatment consists of a combination of a proteasome inhibitor (bortezomib or carfilzomib), with an immunomodulatory drug (thalidomide or lenalidomide) and dexamethasone for 4 to 6 cycles. In Brazil, patients receive mostly VTD (bortezomib, thalidomide, and dexamethasone) or VCD (bortezomib, cyclophosphamide, and dexamethasone). Since July 2019, daratumumab in combination with VTD has been approved in Brazil. The approval was based on Cassiopeia study that showed superiority of daratumumab combination compared to VTD alone to achieve stringent complete remission (primary endpoint) and progression-free survival [3]. Lenalidomide as maintenance therapy after ASCT until progression has also been approved in Brazil, but the access remains a significant concern [4]. For non-eligible to ASCT patients, we recommend stratification based on the frailty score preconized by the IMWG at first [5]. For unfit patients, our recommendation is doublet combination with bortezomib or lenalidomide plus dexamethasone. For a fit and intermediate fit patient, a more intensive approach can be chosen. Combinations, including three or four drugs can be an option. VRD (bortezomib, lenalidomide and dexamethasone) was approved in Brazil supported by SWOG data reporting superiority of this combination compared to RD alone in terms of progression-free survival and overall survival [6]. In 2018, DARA-VMP (daratumumab, bortezomib, melphalan, and prednisone) was also approved in Brazil. In this case, based on an improvement of PFS when compared to VMP alone reported by the Alcyone trial [7]. In a relapse setting, we support that a new line of treatment decision should take disease's, previous treatment, and patient's factors into consideration. Important factors that are included in this analysis: aggressiveness of the current relapse, type of prior therapies and their responses, age, frailty, and performance status in the moment of relapse [8]. Since 2015, robust data regarding doublet versus triplet regimens have been published. Combination of lenalidomide and dexamethasone or bortezomibe and dexamethasone, as control group, were compared to combination of carfilzomib lenalidomide and dexamethasone (ASPIRE trial) [9]; ixazomib, lenalidomide and dexamethasone (TOURMALINE trial) [10]; elotuzumab, lenalidomide and dexamethasone (ELOQUENT trial) [11]; daratumumab, bortezomib, dexamethasone (CASTOR trial) [12]; and daratumumab, lenalidomide, dexamethasone (POLLUX trial) [13]. In all these trials, results confirmed that triplet regimens were superior in terms of overall response rate and progression-free survival. After trial publications, the Brazilian Regulatory Agency approved these regimens for MM relapse, but also here access remains the primary barrier. In conclusion, despite there are many approved options for MM treatment from the first line until relapses, universal access is not a reality in our country. The balance of innovative drugs and cost is a critical issue and a big challenge in MM treatment.

References

[1] Rajkumar SV. Multiple myeloma: every year a new standard? Hematol Oncol 2019;37 Suppl 1:62–65.
[2] Gay F, Engelhardt M, Terpos E, et al. From transplant to novel cellular therapies in multiple myeloma: European Myeloma Network guidelines and future perspectives. Haematologica 2018;103:197
[3] Moreau P, Attal M, Hulin C, et al. Bortezomib, thalidomide, and dexamethasone with or without daratumumab before and after autologous stem-cell transplantation for newly diagnosed multiple myeloma (CASSIOPEIA): a randomised, open-label, phase 3 study. Lancet 2019;394:29–38.
[4] McCarthy PL, Holstein SA, Petrucci MT, et al. Lenalidomide maintenance after autologous stem-cell transplantation in newly diagnosed multiple myeloma: a meta-analysis. J Clin Oncol 2017;35:3279.
[5] Engelhardt M, Dold SM, Ihorst G, et al. Geriatric assessment in multiple myeloma patients: validation of the International Myeloma Working Group (IMWG) score and comparison with other common comorbidity scores. Haematologica 2016;101:1110–9.
[6] Durie BG, Hoering A, Abidi MH, et al. Bortezomib with lenalidomide and dexamethasone versus lenalidomide and dexamethasone alone in patients with newly diagnosed myeloma without intent for immediate autologous stem-cell transplant (SWOG S0777): a randomised, open-label, phase 3 trial. Lancet 2017;389:519–527.
[7] Mateos MV, Dimopoulos MA, Cavo M, et al. ALCYONE Trial Investigators. Daratumumab plus Bortezomib, Melphalan, and Prednisone for Untreated Myeloma. N Engl J Med. 2018;378:518–528.
[8] Laubach J, Garderet L, Mahindra A, et al. Management of relapsed multiple myeloma: recommendations of the International Myeloma Working Group. Leukemia 2016;30:1005.
[9] Stewart AK, Rajkumar SV, Dimopoulos MA, et al. Carfilzomib, lenalidomide, and dexamethasone for relapsed multiple myeloma. N Engl J Med 2015;372:142.
[10] Moreau P, Masszi T, Grzasko N, et al. Oral ixazomib, lenalidomide, and dexamethasone for multiple myeloma. N Engl J Med 2016;374:1621.
[11] Lonial S, Dimopoulos M, Palumbo A, et al. Elotuzumab therapy for relapsed or refractory multiple myeloma. N Engl J Med 2015;373:621
[12] Palumbo A, Chanan-Khan A, Weisel K, et al. Daratumumab, bortezomib, and dexamethasone for multiple myeloma. N Engl J Med 2016;375:754.
[13] Dimopoulos MA, Oriol A, Nahi H, et al. Daratumumab, lenalidomide, and dexamethasone for multiple myeloma. N Engl J Med 2016;375:1319.

SP-22

Importance of minimal disease detection in multiple myeloma

Evangelos Terpos
National and Kapodistrian University of Athens, School of Medicine, Athens, Greece

The novel response criteria in antimyeloma therapy, published by the International Myeloma Working Group (IMWG), include minimal residual disease (MRD) assessment in multiple myeloma (MM), aiming to identify better definitions of complete response (CR) than those traditionally defined by conventional methods. With the use of flow cytometry or gene sequencing for the identification of residual tumor cells in the bone marrow and sensitive imaging techniques to detect the presence of extramedullary residual disease, the IMWG has defined new response categories that will hopefully contribute to the uniform reporting within and outside clinical trials, to a better evaluation of treatment efficacy and also to help optimizing patient treatment according to the risk of relapse, particularly during consolidation or maintenance phases of therapy.

So far, several, non-published, clinical trials have randomized MM patients according to their MRD status, in order to investigate the role of MRD to individualize therapy. Overall, the experience of several cooperative groups using different MRD techniques indicates that persistence of MRD is always an adverse prognostic feature, even among CR patients. Consequently, it would be safer to take clinical decisions based on MRD-positivity rather than on MRD-negativity, since the patchy pattern of BM infiltration typically observed in MM leads to a degree of uncertainty regarding MRD-negative results: does this guarantee absence of tumor cells or is it the result of a non-representative BM sample due to patchy tumor infiltration? Many studies have shown the value of MRD to evaluate the efficacy of specific treatment phases and therefore, to support potential treatment decisions. For example, both the Spanish PETHEMA and the UK MRC study groups have shown that MRD kinetics before and after HDT/ASCT allow identification of chemosensitive versus chemoresistant patients. For the latter, it could be hypothesized that consolidation with alternative therapies would be needed to improve outcomes. Following consolidation, physicians face another treatment decision: maintenance versus no maintenance and duration? Ladetto et al. reported PFS rates of 100% vs. 57% for patients in molecular-CR vs. MRD-positive cases after consolidation, respectively. Since no maintenance therapy was given in the GIMEMA VEL-03-096 study, one might hypothesize that for those cases failing to reach MRD-negativity despite being in CR/nCR after consolidation, maintenance may represent an effective approach to eradicate MRD-levels and improve outcome. Accordingly, Rawstron et al. have shown

that one out of four MRD-positive patients randomized to the maintenance arm of the MRC-myeloma IX (intensive) study turned into MRD-negative and experienced significantly prolonged PFS vs. the abstention arm. However, because even MRD-negative patients receiving maintenance continue to show late relapses, it may be envisioned that we need to increase the sensitivity of MRD techniques to better monitoring "theoretically MRD negative" patients during maintenance therapy; moreover, if treatment decisions are taken according to patients' MRD status, follow-up MRD studies would also become useful to detect MRD reappearance preceding clinical relapse. This approach is likely to imply serial MRD assessment which, at the moment, would require the need of invasive and inconvenient multiple BM aspirates. Most recently, NGS has been evaluated in PB (i.e. plasma) from MM patients after induction and this would represent an attractive minimally invasive approach. However, preliminary data indicates that clonotypic sequences identified at baseline, become undetectable with just a few cycles of chemotherapy, even among electrophoresis positive patients. Thus, further research is warranted to establish the feasibility of PB (e.g. cell- or free DNA-based) MRD monitoring. Furthermore, our knowledge on clonal tiding (i.e.: disappearance of pre-existing or occurrence of new clones), during maintenance or progression-free periods without therapy is very limited if existing at all, and the concept of clonal tiding should also be taken into consideration while designing such treatment strategies.

The choice of MRD technology for monitoring will depend on how individual centers' priorities adjust to the specific advantages that each tool has to offer. In turn, extensive research is still warranted to determine how to best integrate medullary and extramedullary MRD monitoring. In other hematological malignancies, baseline risk-factors and MRD monitoring have an established and complementary role to individualize treatment. Over the last two decades, several groups have consistently confirmed the added value of MRD in MM, and the time has come to establish the role of baseline risk-factors plus MRD monitoring for tailored therapy. This requires the introduction of standardized, highly sensitive, cost-effective, and broadly-available MRD techniques in clinical trials.

SP-23

Therapeutic modulation of pleural effusion environment: the Next-Gen immunotherapy

Vera S. Donnenberg
University of Pittsburgh School of Pharmacy, Pittsburgh, PA, USA

Introduction: At advanced stages, metastatic cancer infiltrates lymph nodes in the chest as well as the lining of the chest cavity, known as the pleura. When this occurs, the normal cycle of fluid secretion and absorption is interrupted, resulting in unopposed collection and compression of the lung. The fluid, termed malignant pleural effusion (MPE), is composed of proteins, cytokines, chemokines, cancer cells, and lymphoid and myeloid immune cells. Accumulation of this fluid in the pleura results in symptoms that range from cough or dyspnea to life threatening breathlessness and hypoxia. MPE are a common terminal pathway for many cancers, affecting millions of patients world-wide. MPE is an aggressive disease with poor prognosis. Because there is no effective treatment the life expectancy is only 3–12 months [1]. Therefore, there is a pressing unmet need for an effective targeted therapy. From studies examining MPE palliation, epithelial cancers account for about 80% of patients receiving palliative interventions for their MPE. Despite recent success of immunotherapeutic approaches to metastatic cancer, these modalities have thus far been ineffective in the setting of MPE.

Results: Here we will discuss how the immune milieu of pleural metastases conditions the pleural space as a tumor-promoting, wound healing environment, despite an abundance of potential antigen presenting and effector T cells. We and others show that the pleural space is an anatomically confined compartment in which tumor growth-promoting cytokines and chemokines are concentrated, and M2like and Th-2-like immune polarization is enforced, driving the invasive tumor behavior. Even patients that are receiving immune checkpoint inhibitors such as anti-PD1 (pembrolizumab, nivolumab) or antiPD-L1 (atezolizumab) therapeutics, can develop MPE which is refractory to these treatments. Further, chimeric antigen receptor T cells (CAR-T) specific to mesothelin are being tested intrapleurally [2] in patients with mesothelioma-MPE but not all patients respond. This may be due to several factors such as a loss of antigen (mesothelin), lack of co-stimulatory molecule expression on pleural macrophages, or suppression CAR-T effector function by the pleural environment. Based on our findings of the suppressive secretome of the MPE [3], we propose that local immune repolarization must accompany immune checkpoint or cellular therapy to successfully eradicate pleural tumor.

Conclusions: The routine use of pleural catheters for MPE drainage provides the opportunity for local administration of antibody and cellular therapeutics as well as for non-invasive sequential sampling of the pleural environment [4]. We propose that the rich cellular composition of MPE can be turned into an effective anti-tumor-specific environment when localized immune repolarization is achieved. We also argue that a combination of local repolarizing therapy in combination with immune checkpoint blockade may be optimal for generation of an effective systemic anti-tumor response.

References

[1] Clive AO, et al. Predicting survival in malignant pleural effusion: development and validation of the LENT prognostic score. Thorax 2014.
[2] Adusumilli PS, et al. A phase I clinical trial of malignant pleural disease treated with regionally delivered autologous mesothelin-targeted CAR T cells: safety and efficacy. In AACR Annual Meeting. 2019. Atlanta, GA: American Association for Cancer Research.
[3] Donnenberg AD, et al. Treatment of malignant pleural effusions: the case for localized immunotherapy. J Immunother Cancer 2019;7(1):110.
[4] Suzuki K, et al. Palliation and pleurodesis in malignant pleural effusion: the role for tunneled pleural catheters. J Thorac Oncol 2011;6(4):762–7.

SP-24

The secretome of malignant pleural effusions: clues to targets of therapy

Albert D. Donnenberg
Department of Medicine, Division of Hematology-Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

Objective: We compared the secretome of pleural effusions (PE) from 18 different malignancies, benign effusions and the published plasma profile of patients receiving chimeric antigen receptor T cells (CAR-T) [1], to determine factors unique to neoplasia in PE and those accompanying an efficacious peripheral anti-tumor immune response (CAR-T).

Methodology: Cryopreserved cell-free pleural effusion (PE) fluid from 356 PE were assayed for a panel of 40 of cytokines/chemokines using the Luminex system.

Results: Profiles of benign and malignant PE were dominated by high concentrations of sIL-6Rα, CCL2/MCP1, CXCL10/IP10, IL-6, TGFβ1, CCL22/MDC, CXCL8/IL-8 and IL-10. Malignant PE contained significantly higher concentrations of CX3CL1/fractalkine, IL-1Rα, VEGF, CCL4/MIP1β, FGF2, IL-12p40, IFNγ, IL-1α, IFNα2, and TNFβ. Effector cytokines IFNγ, IFNα2, and TNFβ were higher than in benign PE across most, but not all malignancies. Comparing malignant PE and published plasma levels of CAR-T recipients, both were dominated by sIL-6Rα and IL-6 but malignant PE had more VEGF, FGF2 and TNFα, and less IL-2, IL-4, IL-13, IL-15, MIP1α and IFNγ.

Conclusion: An immunosuppressive, wound-healing environment characterizes both benign and malignant PE. A dampened effector response (TNFα, MIP1α, IFNγ, IFNα2, and TNFβ) was detected in most malignant PE (including breast, lung, esophageal and cholangio CA). The data suggest that the IL-6/sIL-6Rα axis is a central driver of the immunosuppressive, tumor-supportive pleural environment. Despite this hostile environment, there is evidence of a nascent immune effector response that may be harnessed therapeutically by modifying the local pleural immune environment with antibody-based therapeutics, by ex vivo activation and reinstillation of pleural T cells, or both [2]. The CAR-T experience suggests that targeting the IL-6/sIL-6Rα axis by local administration of tocilizumab is a logical starting point.

References

[1] Teachey DT, et al. Identification of predictive biomarkers for cytokine release syndrome after chimeric antigen receptor t-cell therapy for acute lymphoblastic leukemia. Cancer discovery 2016;6(6):664–79.

[2] Donnenberg AD, et al. Treatment of malignant pleural effusions: the case for localized immunotherapy. J Immunother Cancer 2019;7(1):110.

SP-25

Are maintenance post-transplant therapies needed?

Khalid Halahleh
King Hussein Cancer Center

Disease recurrence is a major cause of transplant failure and is associated with poor prognosis. One strategy to prevent relapse is maintenance therapy which can be given to everyone or just persons at increased relapse risk such as those with measurable residual disease posttransplant. To be effective posttransplant maintenance therapy should be safe when given soon after a transplant.

Hypo-methylating drugs are safe and effective therapy of older persons with higher-risk myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML). Their mechanism of action is unknown. One effect is to increase expression of epigenetically silenced potentially leukaemia-related or even -specific antigens which might induce an immune response. Several retrospective studies claim decreased relapse risk when used prophylactically and/or preemptively but there are no confirmatory randomized trials. There are also no retrospective or RCTs supporting use of a *FLT3*-inhibitor posttransplant to prevent relapse. Two small, uncontrolled retrospective analyses reported better leukaemia-free survival (LFS) compared with historical controls. Again, there are no convincing data from a large RCT.

Several retrospective analyses report better outcomes in subjects with *BCRABL1*-positive acute lymphoblastic leukaemia (ALL) receiving posttransplant tyrosine kinase-inhibitors. In a small RCT the GMALL study group compared use of imatinib prophylactically versus pre-emptively (MRD-test-positive). Outcomes were similar. Analysis of an observational database by the EBMT Acute Leukemia Working Party reported fewer relapses in subjects receiving a TKI posttransplant (HR= 0.4; P=0.01). Confirmation in a RCT is needed.

These data hint at a possible benefit of posttransplant maintenance in MDS, AML and ALL. However, none of these data are convincing. Nor will anyone be convinced of safety and efficacy of posttransplant maintenance absent data from a large RCT.

References

[1] Jabbour E, Giralt S, Kantarjian H, et al. Low-dose azacitidine after allogeneic stem cell transplantation for acute leukemia. Cancer 2009
[2] Guillaume T, Malard F, Magro L, et al. Prospective phase II study of prophylactic low-dose azacitidine and donor lymphocyte infusions following allogeneic hematopoietic stem cell transplantation for high risk acute myeloid leukemia and myelodysplastic syndrome. Bone Marrow Transplant 2019; doi:10.1038/s41409-019-0536-y.
[3] Metzelder SK, Schroeder T, Finck A, et al. High activity of sorafenib in FLT3-ITD-positive acute myeloid leukemia synergizes with allo-immune effects to induce sustained responses. Leukemia 2012;26:2353–9.
[4] Sato T, Yang X, Knapper S, et al. FLT3 ligand impedes the efficacy of FLT3 inhibitors in vitro and in vivo. Blood 2011;117:3286–93.
[5] Chen YB, Li S, Lane AA, et al. Phase I trial of maintenance sorafenib after allogeneic hematopoietic stem cell transplantation for fms-like tyrosine kinase 3 internal tandem duplication acute myeloid leukemia. Biol Blood Marrow Transplant 2014;20:2042–8.
[6] Battipaglia G, Massoud R, Ahmed SO, et al. Efficacy and feasibility of sorafenib as a maintenance agent after allogeneic hematopoietic stem cell transplantation for Fms-like tyrosine kinase 3 mutated acute myeloid leukemia: an update. Clin Lymphoma Myeloma Leuk 2019;pii :S2152-2650(19)30109-0.
[7] Pratz KW, Ivana G, Karp JE, et al. Prospective study of peri-transplant use of sorafenib as remission maintenance for FLT3-ITD patients undergoing allogeneic transplantation. Blood 2015;126:3164.
[8] Stone RM, Mandrekar S, Sanford BL, et al. The multi-kinase inhibitor midostaurin (M) prolongs survival compared with placebo(P) in combination with daunorubicin (D)/cytarabine (C) induction (ind), high-doseC consolidation (consol), and as maintenance (maint) therapy in newly diagnosed acute myeloid leukemia (AML) patients (pts) age 18-60 with FLT3 mutations (muts): an international prospective randomized (rand) P-controlled double-blind trial (CALGB 10603/RATIFY [Alliance]). Blood 2015;126:6.
[9] Nishiwaki S, Miyamura K, Kato C, et al. Impact of post-transplant imatinib administration on Philadelphia chromosome-positive acute lymphoblastic leukaemia. Anticancer Res 2010;30(6):2415–8.
[10] Kebriaei P, Saliba R, Rondon G, et al. Long-term follow-up of allogeneic hematopoietic stem cell transplantation for patients with Philadelphia chromosome-positive acute lymphoblastic leukemia: impact of tyrosine kinase inhibitors on treatment outcomes. Biol Blood Marrow Transplant 2012;18(4):584–92.
[11] Pfeifer B, Wassmann W, Bethge J, et al. Randomized comparison of prophylactic and minimal residual disease-triggered imatinib after allogeneic stem cell transplantation for BCR–ABL1-positive acute lymphoblastic leukemia. Leukemia 2013;27:1254–62.
[12] Shimoni A, Volchek Y, Koren-Michowitz M, et al. Phase 1/2 study of nilotinib prophylaxis after allogeneic stem cell transplantation in patients with advanced chronic myeloid leukemia or Philadelphia chromosome-positive acute lymphoblastic leukemia. Cancer 2015;121(6):863–71.
[13] Giebel S, Czyz A, Ottmann O, et al. The use of tyrosine kinase inhibitors to prevent relapse after allogeneic hematopoietic stem cell transplantation for patients with Philadelphia chromosome–positive acute lymphoblastic leukemia: a position statement of the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation. Bone Marrow Transplant 2019;6:798–809.

SP-26

Will Car T-cell therapy replace hematopoietic stem cells transplant?

Francesco Saglio
Regina Margherita Children's Hospital, Torino, Italy

Chimeric antigen receptor (CAR)-T cell therapy is emerging as one of the most powerful and promising therapeutic tool for the treatment of neoplasia. CAR-T cells are T-lymphocytes modified in vitro to harbor an artificial molecular construct (CAR) made by an extracellular domain consisting of a single-chain variable fragment (scFv) recognizing a specific tumor antigen joined to a transmembrane domain which is linked to the signaling unit CD3ζ and co-stimulatory units CD28 or 4-1BB of the T-cell receptor, making them capable to recognize and to kill tumor's cell in a HLA-independent manner.

CAR T-cell therapy consists in the selection of patient's normal T-cells via leukapheresis, activation, transduction to express CARs using lentiviral or retroviral vectors, expansion of transduced cells and infusion of the final product back to the patient. After the CAR T-cells are infused back into the patient, the engineered cells proliferate, recognize and kill tumor cells bearing the specific antigen the CAR is directed against. Most of the current clinical trials have been with anti-CD19 CAR T-cells directed against the antigen CD19, mainly expressed by acute lymphoblastic leukemia and B-cells non-Hodgkin lymphomas.

There have been 3 recent US Food and Drug Administration (FDA) approvals for using antiCD19 CAR T-cells in B-Cell malignancies and this technology is moving from an experimental approach available for very selected patients treated in a small number of Centers to a standard-of-care therapy available almost worldwide.

The diffusion of this technology requires a re-definition of the role of all the other therapy options currently available including other forms of immuno-therapy as monoclonal antibodies, bi-specific monoclonal antibodies and, upon all, allogeneic hematopoietic stem cell transplantation (alloHSCT).

Until now data are limited and the question If CAR-T cells therapy will re-place alloHSCT in the future is far from being answered but there are some observations derived from pivotal clinical trials that probably will help us in building future trials aimed to define this topic.

The first point is about the toxicity: alloHSCT is related to a well know acute and delayed toxicity; CAR-T cells are characterized by some peculiar side effects as the Cytokines Release Syndrome or CNS toxicity that if are not properly detected and treated may lead to very severe consequences with a

significant mortality rate. Moreover, since the follow up is not very long data about long term effects are lacking.
The second point is represented by the persistence of these cells in the patients that is related to the definition of the need for patients responding to CAR-T cells to proceed in any case to alloHSCT to consolidate disease remission.
Finally, some technological, practical and economical considerations need to be defined in order to extend the use of this technology worldwide, in respect to alloHSCT.

SP-27
Oral chronic graft-versus-host disease

Nathaniel S. Treister
Brigham and Women's Hospital, Boston, USA; Harvard School of Dental Medicine, Boston, USA

Chronic graft-versus-host disease (cGVHD) is a major complication of allogeneic hematopoietic cell transplantation that can have a tremendous impact on quality of life. The oral cavity is frequently affected by cGVHD and is often a site of prominent disease activity. Clinical features include lichenoid mucosal inflammation, salivary gland dysfunction, and sclerodermatous changes, contributing to mouth pain and sensitivity, xerostomia and dental caries, and reduced mouth opening and compromised function. Localized and ancillary therapies can be effective in reducing symptoms, increasing salivary function and reducing the risk of dental caries, and improving oral function. Healthcare providers must anticipate and recognize the oral manifestations of cGVHD and be able to establish a diagnosis and provide effective basic management. Furthermore, patients with cGVHD are at significantly increased risk for developing oral squamous cell carcinoma and require lifelong clinical surveillance.

SP-28
CAR T therapy for solid tumors

Prasad Adusumilli
Memorial Sloan-Kettering Cancer Center, NY

"A two-in-one approach to target solid tumors - CAR T cells and checkpoint blockade" will focus on the advances in CAR T-cell therapy in preclinical arena, translation to treat solid tumor patients and our recent results from Mesothelin-targeted CAR T-cell therapy trials for patients with thoracic cancers. Strategies to overcome hurdles in solid tumor cell therapy will be discussed.

SP-29
HPV-associated head/neck cancer: new stagings and new treatments

Kübra Özkaya Toraman
Afyon Kocatepe University, Faculty of Medicine, Department of Radiation Oncology

The AJCC/UICC Oropharyngeal Cancer Staging 8th Edition became the third cancer staging algorithm (after prostate and esophagus) deviating from the classical anatomy-based model with its HPV(+) patient-specific classification. This was a combined result of the steady increase in the HPV(+) OPC incidence being observed since the '90s, different demographical characteristics with better prognosis and treatment responses of this patient group and mostly, the evident failure of former staging remarked by the insignificant differences in the survival rates of HPV(+) Stage I-II-III-IVa patient groups.
The suggestion of HPV(+) OPC specific staging gave rise to the questions about (and, of course, clinical studies for) the most proper way of HPV diagnosis and the necessity and methodology of de-escalation of the treatment because of relatively better prognosis and treatment responses. The 8th edition of TNM now mandates p16 immunohistochemical staining, with its reliability, affordability, availability, and interpretability as the surrogate marker of HPV related disease.
New HPV specific staging does not include a "Tis" stage because of the non-aggressive character of this tumor type and lack of a distinct basal membrane in the epithelium of Waldeyer Ring. Because of indistinguishable curves of former T4a and T4b stages, they are now combined as T4. Other than these two, T stage for HPV(+) group remained same. On nodal staging, clinic and pathological staging were separated. According to clinical staging, ipsilateral metastatic lymph nodes are N1; contra- and bilateral lymph nodes are N2, any lymph nodes >6 cm is N3. Pathological staging focused on the number of metastatic lymph nodes. While the extra-nodal extension of the tumor is a valid criterion for other tumor types, for HPV(+) patients, it is disregarded since their effect on prognosis is unclear. Prognostic groups were changed completely. Now, only the patients with distant metastasis are accepted as stage 4.
There is still no consensus about the treatment de-escalation since the different trials on different de-escalation strategies showed mixed results. Some of de-escalation strategies under investigation are as follows: Radiation-cetuximab combination instead of cisplatin, decreasing radiation doses or/volumes for the patient who respond induction chemotherapy well, radiation alone instead of chemoradiation, transoral surgery followed or not postoperative radiotherapy.

SP-30
Immune precision medicine in cancer

Jean-François Rossi
Institut Sainte Catherine, Avignon and University of Montpellier, France

Precision medicine has been defined by the National Institute of Health as "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person". So, Precision Medicine is preferable to Personalized Medicine. Immune Precision Medicine is not only when immune therapy meets precision medicine but it also encompasses a better biological understanding of the tumor cells and its microenvironment, an evaluation of the immune control mechanisms, including immune senescence/exhaustion, within a bio-clinical overview, to define a personalized therapeutic strategy. Cancer cell growth is associated to an immune surveillance failure and the aim to restore an immune control of cancer cells represents a major therapeutic development. Cancer immunotherapy can be envisaged by the following four strategies to block the tumor immune evasion and to restore immune surveillance: 1) increasing the number of immune effector cells (IEC) by infusing ex-vivo expanded IEC to improve the IEC/tumor cell ratio; 2) increasing the IEC recognition affinity to tumor antigens or tumor-associated-antigens (TAA); 3) improving the accessibility of killer IEC to the cancer cells through its microenvironment by lowering the mechanisms of immune failure; 4) blocking the immune suppression ability of cancer cells. These may restore the immune surveillance by not only killing the tumor cells but also preventing the emergence of new tumor cell clones which may result due to gene mutation after anti-tumor therapy. One of the most important historical successes in immune therapy is represented by monoclonal antibodies, particularly the use of rituximab for B-cell lymphoproliferative disorders. More recently, other monoclonal antibodies have been developed, to inhibit immune checkpoints within the tumor microenvironment that limit immune suppression, or to enhance some immune functions with immune adjuvants through different targets such as Toll-receptor agonists. The aim is to inhibit cancer growth proliferation, a situation that could be biologically measured by the diminishing/elimination of cancer residual cells, and clinically by improving the response duration with no or few adverse effects. This effect is supported by enhancing the number, the functions, and the activity of the IECs, including natural killer (NK) lymphocytes, NKT-lymphocytes, gdT-lymphocytes, cytotoxic T-lymphocytes; directly or indirectly through vaccines particularly with neoantigens, engineered chimeric antigen receptor (CAR) T lymphocytes and by lowering the functions of the immune suppressive cells. Beyond these new therapeutics and their personalized usage, new considerations have to be taken into account, such as epigenetic regulation particularly from microbiota, evaluation of transversal functions, particularly cellular metabolism, and consideration to the clinical consequences at the body level.

Reference

[1] Rossi JF, et al. Immune precision medicine for cancer: a novel insight based on the efficiency of immune effector cells. Cancer Comm 2019;39(1):34.

SP-31

Evolving approaches in systemic therapy for triple-negative breast cancer in neoadjuvant and adjuvant settings

Özlem Er
Acıbadem MAA University Maslak Hospital, Istanbul, Turkey

Triple-negative breast cancer (TNBC) accounts for 15–20% of diagnosed breast tumours, with higher incidence in young women, and it is frequently associated with BRCA germline mutations. Chemotherapy is the only well-established therapeutic option in both early- and advanced-stages of the disease. TNBC tumours relapse earlier after standard anthracycline- and/or taxane-based chemotherapy treatments, generally within 1–3 years after the diagnosis, and often develop visceral metastases, representing the subtype with a worse prognosis among all breast cancers. The advent of gene expression micro-array technology has led to the identification of different actionable targets including various genomic alterations, androgen receptor, PARP, PI3K, VEGF and other proteins of the angiogenic pathway. Novel targeted drugs have been tested in clinical trials reporting promising results in specific TNBC molecular subgroups. Cytotoxic chemotherapy remains the mainstay of treatment for TNBC patients. Adjuvant and neoadjuvant therapy are basically equivalent in terms of long-term outcomes. However, neoadjuvant treatment can provide other benefits. Neoadjuvant therapy can allow for better outcomes in terms of local results — some patients with bigger, more advanced tumors may become more likely to be surgically operable or have better cosmetic results with systemic therapy prior to surgery. In addition to benefits for individual patients, neoadjuvant treatment can also allow for more detailed research into the biology of predictors of treatment response. Promising novel strategies, among them immune checkpoint inhibitors, are currently under clinical investigation.

SP-32

Overcoming the resistance in HER2(+) metastatic breast cancer

Sernaz Uzunoğlu
Trakya University Hospital, Edirne, Turkey

HER2(+) tumors account for 20–30% of breast cancers, and these tumors are usually aggressive with short life expectancy. In the last two decades, directed therapies against HER2 such as monoclonal antibodies, tyrosine kinase inhibitors and antibody-drug conjugates (ADC) became a very important part of the therapy and improved the prognosis of the patients especially in the metastatic setting. But primary or acquired resistance to anti HER2 therapies are still the most challenging problem of this treatment process.

In recent years several resistance mechanisms have been identified, however only a few of them have been validated in clinical studies, and their reliability and clinical usefulness remain unclear. The mechanisms of resistance and response heterogeneity to antiHER2 therapy include; incomplete blockage of HER2 receptor, activation of parallel or downstream pathways, alternative RTKs or other membrane receptors outside the HER family. Other intracellular mechanisms involved in resistance to HER2 therapy consist in: cross-signalling to HER2 (HER2 heterodimer, ER expression), activation of cyclin-D1-dependent kinase 4/6 (CDK 4/6) axis, fatty acid synthase overexpression (FASN), escape from ADCC, dysregulation of the cell cycle.

Theoretically, majority of resistance mechanisms could be targeted by agents that are already available such as inhibitors of ER, PI3KA/mTOR, EGFR1. But understanding mechanisms of resistance and their clinical implications regarding response to treatment is extremely complex and a wide range of mechanisms of resistance may coexist in the same cell. Moreover, the discovery of predictive biomarkers beyond HER2 will help us to better select patients and improve their outcomes.

To overcome or delay resistance to antiHER2 treatments, many novel additional therapeutic strategies are being developed such as novel HER2 antibodies (margetixumab, MCLA-128,ZW25 (bispecific antibodies)), new antibody-drug conjugates (SYD 985, DS-8201,MM-301), novel TKIs (neratinib, tucatinib, pyrotinib, poziotinib), combinations of antiHER2 agents with immunotherapy or CDK 4/6 inhibitors or PI3K/AKT/mTOR inhibitors.

All these promising treatments and combinations will probably improve quality of life and survival of metastatic HER2 positive breast cancer patients. Moreover, the coexistence of different resistance mechanisms, as a result of intralesional or interlesional heterogeneity, may prevent the possibility to contemporaneously target all resistant tumor clones. In order to target the most relevant mechanisms in individual patients, after each progression there might be a better assessment of the evolving changes of the tumor in real time that will help to better understand mechanisms of resistance, such as the analysis of circulating tumor DNA or circulating tumor cells.

SP-33

Small round cell tumors

Kıvılcım Eren Erdoğan
Çukurova University

Small round cell tumors of bone and soft tissue are heterogenous group of tumors despite their similar morphology. They are composed of monotonous small round cells with scant cytoplasm with ill-defined borders. Some tumors display specific morphological clues such as chromatin pattern (CIC rearranged sarcoma, poorly differentiated synovial sarcoma, alveolar rhabdomyosarcoma, etc.); stromal changes (desmoplastic small round cell tumor, CIC rearranged sarcoma, alveolar rhabdomyosarcoma, etc.), rosette formation or vessel architecture. But these changes are so subtle and it is not always possible to do differential diagnosis under light microscope. Immunohistochemistry is an ancillary method to specify the origin of the cell type. The advised panel includes CD99, Desmin, CD45, TDT, WT1, TLE1, keratin, Myogenin, S100. Molecular data support distinct small round cell tumors which behave different from morphologically similar counterparts. Ewing sarcoma (ES) and so called 'atypical' ES are the best examples of genetically distinctive tumors. The molecular alterations are important for diagnosis as well as prognosis. Distinction of small round cell tumors are not important only for definitive diagnosis but also for management of the patients

SP-34

Transplant activities, experience

Malek Baassiri
Makassed General Hospital, Beirut, Lebanon

Lebanon is a low-to middle income country as classified by the World Bank. The number of pediatric malignancies is increasing significantly nowadays. Moreover, the diagnosis of benign hemoglobinopathies, inborn errors of metabolism, primary immunodeficiencies, and bone marrow failure syndromes is improving significantly, with people getting aware of seeking medical advice in addition to high consanguinity rate. As the economical crisis is increasing, the financial support from the government is deficient. Also, the need for some diagnostic testing/imaging for some of the infectious complications are sometimes deficient or the presence of undertrained personnel. Here are some of the cases that had bone marrow transplantation in a tertiary center, Makassed General Hospital, as well of those who didn't have a BMT due to several factors highlighting the problems and the possible solutions.

SP-35

Transplant activities, experience

Lalith Parmar
Sankalp India Foundation an NGO

We share the experience of Sankalp-Cure2Children Network from 3 centres in India with 386 allogenic related bone marrow transplants in last 7 years for non-malignant diseases, mainly severe thalassemia in pediatric population.

Our program works on a hub and spoke model with close collaboration between thalassemia centres located closer to the patients and the transplant centres. The program works to enable improved care and management for thalassemia at the spoke thalassemia clinics. Free HLA typing is offered to all eligible patients who have a prospect of finding a related donor and

those who have a match undergo a program of downstaging using intense transfusion, chelation and hydroxyurea to bring reverse iron overload and organomegaly as much as possible.
The selection of the kid for transplant is based purely on medical eligibility. Transplants are offered on a not-for-profit basis with the cost fixed (USD 11,800 to USD 12,500 for matched related and USD 18,000 for partially matched related) and covers all medical expenses including complications up to 1 year after transplant. Families contribute a part of the fixed cost based upon their financial status and the rest is fundraised. The centre is kept adequately occupied all the time.
The centres part of the program uses the same cloud hosted transplant data management application - BMTPlus. Using digital technologies, the centres have close collaboration pooling skill/expertise, treatment protocols and best practices - fostering effective knowledge management and continuous learning environment. Rigorous quality management is an essential component, which has currently led one of the centres to inspection for FACT/JACIE accreditation. Transplant data is shared electronically and automatically with Centre for International Bone Marrow Transplantation Research (CIBMTR).
Overall survival has been 90% and disease-free survival has been 80% with 7% transplant related mortality. Outcomes have improved successively over the years and the day-100 survival improved from 88.3% to 95.5%, which compares well with the 96.9% day-100 survival reported in USA for thalassemia. Systematic data management and integrated analytics with data pooled for large number of patients has led to several population and context specific findings which have been published shared in prestigious journals and have been shared on international forums.
Our operating model using networking and digital technologies has enabled sustainability around bone marrow transplantation in low-resource settings contributing to increased access and outcomes.

SP-36
CAR-T cell therapy in pediatrics

Patrick Schlegel
Universitätsklinikum Tübingen, Tübingen, Germany

Within the past few years CD19-CAR-T cell therapy has been shown to induce durable remission and cure in heavily pretreated patients with no further standard of care treatment including failure to blinatumomab treatment and allogeneic stem cell transplantation. Consequently, two CD19 CAR-T cell products have been FDA- and EMA-approved and are now available for refractory B-lineage malignancies BCP-ALL in pediatrics and DLBCL in adults. Yet, a small number of patients have already revealed the limitations of CD19 CAR-T cell therapy comprising acute toxicities such as fatal cytokine release syndrome and failure of treatment due to non-engraftment of CAR-T cells, immune mediated rejection of CAR-T cells, non-persistence of CAR-T cells and most important downregulation and loss of the targeted epitope. The challenges have been addressed by sequential CD19 and CD22 CAR targeting and by sophisticated strategies of synchronic combinatorial targeting with promising preliminary results. Moreover, in AML CD33 is targeted by CAR-T cells as a bridge to transplant and in solid cancer GD2 CAR-T cells have proven efficacy in far advanced neuroblastoma patients and EGFR CAR-T cells in recurrent CNS tumors demonstrating general antitumor response but underscoring the obstacles in cancer with heterogenous antigen expression profiles and solid cancer. Further strategies including additional genetic modifications to improve *in vivo* performance, logic CAR systems and adapter CAR-T cell technologies allowing to increase the total cell number and combinatorial approaches are urgently needed to enhance antitumor activity to achieve an immunological cure in the future.

SP-37
Upregulating hemoglobin F using CRISPR/Cas9 gene editing in beta-thalassemia and sickle cell disease

John Chapin
CRISPR Therapeutics, Cambridge, MA, USA

β-hemoglobinopathies such as transfusion-dependent β-thalassemia (TDT) and sickle cell disease (SCD) represent a significant burden of disease worldwide. Transfusion-dependent β-thalassemia results from a severe genetic deficiency of β-globin production that causes the accumulation of unpaired α-globin chains in erythroid precursors, which results in ineffective erythropoiesis and hemolytic anemia. TDT patients require regular red blood cell transfusions for survival. Sickle cell disease is caused by the homozygous inheritance of the E6V point mutation in the β-globin chain, which causes red blood cells to sickle in circulation. These individuals develop recurrent vaso-occlusive events that start in early childhood. Over time, recurrent occlusive events lead to significant damage to the pulmonary and systemic vasculature, CNS, and increase the risk for thrombosis and stroke.
Patients with β-hemoglobinopathies become symptomatic after birth, when adult hemoglobin replaces fetal hemoglobin (HbF) production. This hemoglobin switching occurs within the first 6–12 months of life and involves the expression of BCL11A, a transcription factor that represses γ-globin and thereby prevents production of the HbF tetramer. Data from natural history studies of TDT and SCD individuals who are also affected by hereditary persistence of fetal hemoglobin continue to produce significant quantities of HbF in adulthood, which improves disease severity. Gene editing technology platforms such as CRISPR-Cas9 have the potential to induce permanent genetic modifications in hematopoietic stem cells at a single on-target site with no detectable off-target effects. For gene disruption, the target specificity of the guide RNA (gRNA) allows the Cas9 endonuclease to cut at a precise genetic sequence that induces DNA double strand breaks (DSBs), which are repaired by non-homologous end joining (NHEJ). DSB repair leads to the creation of small insertions and deletions that disrupt sequences required for the expression of a target gene.
We developed a gRNA with high specificity for the erythroid-lineage specific enhancer region of BCL11A. In vitro editing of CD34+ hematopoietic stem cells (HSCs) indicated high (>80%) levels of edited cells and resulting in increased production of γ-globin and HbF in samples from healthy donors and hemoglobinopathy patients. In a xenotransplantation model, edited CD34+ cells maintained the ability to engraft, persist and differentiate into all lineages of mature blood cell types. Homology-dependent and -independent methods were used in combination with deep sequencing to establish the lack of cutting at off-target sites.
These data combined with a favorable toxicology profile supported the initiation of two first-in-human clinical trials (NCT03655678, TDT; NCT03745287, SCD). Eligibility criteria include 18–35 years-of-age with TDT or SCD, and ability to undergo stem cell mobilization, full myeloablation, and autologous bone marrow transplantation. The autologous edited cell product CTX001 is manufactured from CD34+ cells collected after peripheral mobilization, isolation, and electroporation delivery of the gRNA and Cas9. Enrolled patients will undergo myeloablative conditioning followed by CTX001 infusion. Patients will be followed throughout engraftment to 24 months.
Efficacy assessments include the production of HbF and the reduction of disease burden (transfusion requirements in TDT, vaso-occlusive crises in SCD). Safety assessments include engraftment and adverse events. An additional multi-year follow up study is planned to capture long-term safety and efficacy data associated with CTX001.
In conclusion, CRISPR-Cas9 editing of the erythroid lineage-specific transcription factor BCL11A results in increased production of HbF in vitro without detectable off-target effects. BCL11A-edited autologous CD34+ hematopoietic stem cells may represent a functionally curative option for SCD and TDT

SP-38

Novel therapy for relapsed childhood acute lymphoblastic leukemia

Volkan Hazar
Memorial Health Group Medstar Hospital, Antalya

Acute lymphoblastic leukemia (ALL) is the most common cancer in childhood. Although the prognosis of childhood ALL has improved markedly over the past few decades, recurrent ALL is still difficult to treat. The prognosis of the first relapse depends on the time between onset of treatment and relapse, the site of relapse and the immune type of the blasts. Recently, response to treatment evaluated with minimal residual disease (MRD) has also been shown to be an important parameter in both recurrent disease and initially diagnosed patients. By combining all these factors, risk-based treatment approaches were created in the first recurrence. The first standard treatment of ALL recurrence is the intensification of conventional ALL treatment, and success is achieved in approximately 70% of cases. MRD assessment after re-induction is important to determine which patients at standard risk go to hematopoietic stem cell transplantation. However, there is no complete standard treatment for the high-risk group, which accounts for more than half of the recurrence cases. Recent studies have focused on the clonal origin of recurrent ALL, which was initially found in a small group at the time of diagnosis. Clonal selection and alteration can also occur during chemotherapy and may result in different genetic and epigenetic changes, some of which play a role in drug resistance. Due to these characteristics, new therapeutic approaches have been developed and continue to be developed in order to overcome the resistance that may be encountered in standard ALL treatment and to use in the treatment of this group of cases considering the heterogeneous biological background of high-risk ALL. These developments are in the light of the data obtained in ALL genetics of relapse.

Recurrent ALL treatment can be grouped under the following headings: Standard chemotherapy with or without allogenic hematopoietic stem cell transplantation, new chemotherapeutic agents, targeted therapy and immunotherapy (antibody or cellular based).

Standard chemotherapy with or without allogenic hematopoietic stem cell transplantation

Recurrent childhood ALL treatment consists of intensive treatment blocks, which are used in the initial diagnosis and include a combination of non-cross resistance chemotherapy drugs to reduce toxicity and prevent drug resistance. The aim is to achieve the second complete remission (CR). The risk group determination determines whether post-CR treatment should be continued only with chemotherapy or hematopoietic stem cell transplantation. Re-induction treatment after relapse is usually performed with the same 4 drugs (Corticosteroid, Vincristine, Asparaginase and anthracycline) used in the initial treatment. The COG (Children Oncology Group) reported an 81% chance of obtaining CR2 with this combination (68% in early relapse cases and 96% in late relapse). However, after re-induction, only 38% of the cases had an MRD rate of $<10^{-4}$ which is a threshold accepted as a molecular remission. In the more intensive re-induction British protocol (ALL-R3), Mitoxantrone and Idarubicin were compared, and it was observed that Mitoxantrone resulted in significant increases in both overall survival and progression-free survival rates due to the reduction of the relapse rate. The BFM (Berlin-Frankfurt-Münster) group administered a more intensive re-induction treatment by adding medium-dose Methotrexate and high-dose Cytarabine to the 4-drug chemo combination.

The most decisive role in determining the treatment part after obtaining CR2 is MRD. This has been confirmed by various large groups.

New chemotherapeutic agents

Clofarabine: It is a second-generation purine nucleoside analogue and was approved by the FDA in 2004 for relapse/resistant ALL. Although the response rate was 44% in the phase 2 Clofarabine + Cyclophosphamide study performed in the previously intensively treated group, there was no benefit in the COG study containing Clofarabine + high dose Cytarabin (Ara-C) in the second or more recurrent ALL cases. With its usefulness and partly acceptable tolerance, the high-risk group has begun to be used in the treatment of ALL (St.Jude Total Therapy XVI and IntReALL) and the results have not yet been disclosed. Hepatotoxicity limits its use.

Nelarabine: It is a purine analogue that is particularly effective on T lymphocytes. It has been shown to be effective as a single drug treatment in adult and pediatric recurrent ALL cases who had previously received intensive treatment. It has neurological, dose-limiting toxicity. The COG group demonstrated that the addition of Nelarabine to high-risk T-ALL treatment based on the BFM treatment scheme had an acceptable toxicity (mostly peripheral neuropathy) and observed an uneventful survival rate higher in the Nelarabine group. Phase 3 studies of COG have been completed and the results have not been announced yet.

The use of well-known chemotherapeutics in new formulations to reduce toxicity and increase efficacy is emerging as a new approach. For example, liposomal vincristine has received FDA approval for the treatment of adult ALL. Some of the PEG binding molecules are already in use in daily practice (PEG-Asparaginase), while some have already been used in studies (PEG-doxorubicin).

Bortezomib: It is a proteosome inhibitor. Together with chemotherapy and steroids, it has a synergistic effect in the treatment of ALL. Response rates increased to 73% with the addition of Bortezomib in children with precursor B (pB) cell ALL who had previously received intensive chemotherapy. These data were also supported by Italian studies. In the Italian study, the response rate was 72.6%, whereas MRD $<10^{-3}$ was found in 52% of the cases. In the light of these data COG Bortezomib used in combination with re-induction drugs in phase 2 study and observed similar efficacy in pB-ALL and T-ALL cases. The phase 3 COG study is ongoing. Similarly, the BFM group randomly investigated the effect of Bortezomib in induction in the IntReALL HR group. The efficacy of Carfilzomib, a second generation proteosome inhibitor, is under investigation in phase 1-2 studies.

Relapse ALL is one of the genetic changes in the methylation profile of the gene. Therefore, the role of epigenetic regulators [DNA methyl transferase inhibitors (DNMTi) and histone deacetylase inhibitors (HDACi)] in the treatment is being investigated. These drugs are intended to restore gene expression and return to chemosensitivity.

Decitabine: DNA methyl transferase inhibitor.

Vorinostat: Histone deacetylase inhibitor.

In a phase 2 study in adult subjects, the combination of Decitabine and Vorinostat showed an acceptable toxicity and promising response rates, but the combination of these two drugs in a UK-ALL03-type re-induction in pediatric cases led to an unacceptable toxicity.

Targeted therapies

Tyrosine kinase inhibitors: These are pioneering drugs in the treatment of Ph (+) ALL. Their use in the treatment of Ph-like ALL is being investigated. Ruxolitinib studies are continuing in CRLF2, JAK/EPOR and JAK-STAT/MAPK subgroups and Dasatinib in ABL-class subgroup.

Other targeted treatments: PI3K/AKT/mTOR pathway inhibition is one of the new treatment options. mTOR inhibitors (Rapamycin, Evarolimus and Temsirolimus) are often used in combination with re-induction protocols for this pathway inhibition. Study results have not been reported yet.

One of the effective pathways in the development or recurrence of ALL is the RAS pathway. The MEK inhibitor Selumetinib in this pathway has yielded active results in treatment in preclinical studies. The second-generation Flt3 inhibitor Quizartinib is being studied in patients with ALL. Since bcl-2 pathway prevents apoptosis, the efficacy of bcl-2 inhibitors, Navitoclax and Venetoclax, in ALL is being investigated.

Another approach is to correct the deteriorated cell cycle. Palbociclib, CDK6 inhibitor, is used as monotherapy in KMT2A-r acute leukemia. The results of this study have not yet been disclosed.

Immunotherapy

Antibody-based immunotherapy

Blinatumomab: It is an antibody capable of binding to CD19 and CD3 and transmitting T-cell cytotoxicity to lymphoblasts presenting CD19. When used as monotherapy, full responses can also be obtained. In today's practice, it is recommended to be used as a bridge therapy for HSCT in patients with recurrent/resistant, CD19 presenting, Ph-negative ALL. It has some adverse effects such as cytokine release syndrome and neurological toxicity.

Denintuzumab mafodatin: It is a humanized CD19 antibody bound with monomethyl auristatin F (MMAF). When entering into blast, MMAF secretion

occurs and microtubule formation is prevented, the cell cycle stops in G2/M phase and apoptosis develops. Studies have not been finalized yet. It has ocular toxicity.

ADCT-402: It is a humanized anti-CD19 antibody conjugated with Pyrrolobenzodiazepine dimer cytotoxin. Phase 1 study in relapsed/resistant ALL is in progress.

DT2219: It is a bispecific, recombinant, diphtheria toxin-based immunotoxin that recognizes CD19 and CD22-presenting cells. Phase 2 studies are ongoing.

Inotuzumab ozogamicin: It is a novel monoclonal antibody against CD22 conjugated to the toxin Calicheamicin. In phase studies, MRD negative responses were obtained. Cytopenia, fever, hypotension and elevated liver enzymes may occur. Studies are ongoing in children with relapsed/resistant ALL.

Epratuzumab: It is a humanized monoclonal anti-CD22 antibody. It inhibits CD22-presenting cell proliferation and causes phosphorylation of CD22. It causes convulsion and liver enzyme elevations. The studies are still ongoing and the initial results are promising.

Rituximab: It is a chimeric monoclonal CD20 antibody. It causes apoptosis, antibody-dependent cellular and complement-mediated cytotoxicity. Successful results were obtained in mature B cell ALL and Burkitt lymphoma. In de novo Ph-negative, preB ALL, if the CD20 presentation is ≥20%, CR reaches 70% and the overall survival rate reaches 75%.

Ofatumumab: It is a humanized anti-CD20 antibody. In combination with chemotherapy, CR reached 95% and 67% of them were negative for MRD after 1 cycle in the phase 2 study in adults. It may cause liver toxicity.

Obinutuzumab: It a type II humanized anti-CD20 monoclonal antibody. It causes direct cell death and antibody-dependent cellular cytotoxicity. Although there are studies of lymphoma and chronic lymphocytic leukemia, there is no ALL study yet.

Cellular-based immunotherapy

CAR-T-cells (Chimeric antigen receptor-modified T-cells): Cytotoxic T cells are genetically engineered and transformed into cells that present antibodies against the target leukemic antigens. CR was obtained in the first two pediatric recurrent/resistant ALL cases with 1 month use. CAR-T cells have also been shown in the cerebrospinal fluid. CAR-T therapy can be used as a bridge therapy to allogeneic HSCT. It causes cytokine release syndrome and B cell aplasia. Fever and hypotension due to the release of inflammatory cytokines may occur following infusion of cells. Etanercept (anti-TNF) and Tociluzumab (anti IL-6) can be used in the treatment of cytokine release syndrome. There are many marching studies on CAR-T cell therapy.

References

[1] Phelan KW, Advani AS. Novel Therapies in Acute Lymphoblastic Leukemia. Curr Hematol Malig Rep 2018;13:289–99.
[2] Santiago R, Vairy S, Sinnett D, Krajinovic M, Bittencourt H. Novel therapy for childhood acute lymphoblastic leukemia. Expert Opin Pharmacother 2017;18:1081–99.
[3] Pierro J, Hogan LE, Bhatla T, Carroll WL. New targeted therapies for relapsed pediatric acute lymphoblastic leukemia. Expert Rev Anticancer Ther 2017;17:725–36.

SP-39
Epigenetic therapy in childhood acute myeloid leukemias

Alexandr Popa
N.N. Blokhin National Medical Research Center of Oncology, Pirogov Russian National Research Medical University

Background: The results of treatment children with acute myeloid leukemia (AML) are not satisfied yet. The standard chemotherapy allows achieving complete remission in 92–96% of patients, but cumulative incident of relapse (CIR) and event free survival (EFS) are not good yet. Certain cytogenetic abnormalities and gene mutations are well-known and have been recognized in the WHO classification. AML results from collaborating genetic aberrations in at least 2 different classes. Type I aberrations induce uncontrolled proliferation and/or survival of the leukemic cells and are often represented by activating mutations in genes involved in signal transduction pathways. Type II aberrations inhibit cell differentiation and mainly result from genetic aberrations in hematopoietic transcription factors. However, certain aberrations found in AML, including those related to epigenetic deregulation, do not completely fit into the current type I and type II classification. Research into the epigenetic control of gene expression in AML, including histone modifications, DNA methylation, promises better understanding of the biological nature of the disease. The study AML NII DOG 2012 was the first protocol with combination of chemotherapy and epigenetic therapy (ET).

Materials and methods: From 01.2013 to 09.2018 31 pts were enrolled in NII-DOG- AML-2012 study and 52 pts treated with AML BFM 2004. There was no any difference of age, sex, and risks of diseases between two groups. All pts with HR and IR received treatment by 5 courses (AIE, HAM, AI, hAM, HAE) and with SR – 4 courses (AIE, AI, hAM, HAE). Epigenetic therapy based on combination of Valproic acid (VA) during 78 weeks, All Trans Retinoic Acid (ATRA) 1–43 days and for 14 days with the every post induction chemotherapy course and Decitabine 20 mg/m^2 for 5 days in "window" regime in 5 pts and 26 pts got it on days 16–20 from the beginning AIE.

Results: There were neither any toxicity, no decrease of blasts in BM and peripheral blood after Decitabine in "window", one of the 5 patients developed relapse and one died from severe infection, three pts are still alive, and two got haplo-HSCT. All the pts who dot Decitabine on 16–20 days achieved CR after induction comparing to 82.6% who were treated with the same chemo only (p=0.04). 4-years CIR was 26% and EFS – 66.9±12.4% median follow up 42.5±4.4 compare to 54.2±8%, median follow up 41.7±4.3 mo (ns) and OS – 81.2±9.8% median follow up 46.7±7.9 mo vs 71.4±6.6%, median follow up 54.4±4.2 mo (ns). None of the patients with ET got allo-HSCT, but 6 (12%) in group just with chemo dot allo-HSCT.

Conclusion: Thus, epigenetic therapy increases CR count and survival of children with AML. The place of demetilating agent in AML therapy has to be used in aplasia period after the first course of induction on time with minimum blasts count. Probably it is possible to do additional 5-days course of Decitabine after HAM for pts with HR and IR or AI for SR.

SP-40
Update on HLH treatment

Sule Unal
Hacettepe University, Department of Pediatric Hematology, Ankara, Turkey

Hemophagocytosis may accompany various conditions such as infections, malignancies and metabolic disorders, however hemophagocytic lymphohistiocytosis (HLH) is the clinical syndrome of an overstimulated but ineffective immune response associated with hypercytokinemia. HLH could be either primary (genetic) or secondary (acquired). Standard treatment for primary HLH included etoposide, corticosteroids, cyclosporine A, and intrathecal methotrexate in some of the patients (HLH-2004 Study Protocol) and hematopoietic stem cell transplantation (HSCT) preferably after achievement of remission in active disease. However, in recent years, there is increasing evidence for the effectiveness of less toxic targeted therapies prior to HSCT. On the other hand, treatment of secondary HLH is usually determined on patient's underlying condition.

Recently reported results in a group of 369 patients treated according to the HLH-2004 study indicated that at 5.2 years of follow-up, 62 percent remained alive [1].

Emapalumab, a monoclonal antibody directed against IFNγ which was tested for the treatment of HLH in a phase II/III clinical trial (NCT01818492) has been shown to be effective in patients who were refractory to conventional treatment [2]. Of 16 patients enrolled (median age, 1.2 years), 13 patients completed treatment and 9 achieved a response with achievement to reach HSCT.

Ruxolitinib, an inhibitor of JAK1 and JAK2, can block signaling downstream of IFNγ, IL-6, IL-10, and other cytokines. Case reports on successful results [3] and an ongoing Phase I trial (NCT02400463) is present.

Alemtuzumab, a monoclonal antibody directed against CD52, which depletes T cells, B cells, and monocytes have been shown to be effective in refractory HLH cases with a 77% of patients survived to undergo HSCT [4].

Additionally, targeting of IL-6 by tocilizumab, is also being tested.

Blockade of IL-1 with IL-1 receptor antagonist (anakinra) has been reported to be therapeutic for patients with secondary HLH related to juvenile idiopathic arthritis.

There is accumulating evidence for the efficacy of less toxic targeted therapies.

References

[1] Bergsten E, Horne A, Aricó M, et al. Confirmed efficacy of etoposide and dexamethasone in HLH treatment: long term results of the cooperative HLH-2004 study. Blood 2017;130:2728–38.
[2] Jordan M, Locatelli F, Allen C, et al. A novel targeted approach to the treatment of hemophagocytic lymphohistiocytosis (HLH) with an anti-interferon gamma (IFNγ) monoclonal antibody (mAb), NI-0501: first results from a pilot phase 2 study in children with primary HLH. Blood 2015;126:LBA-3.
[3] Sin JH, Zangardi ML. Ruxolitinib for secondary hemophagocytic lymphohistiocytosis: first case report. Hematol Oncol Stem Cell Ther 2017; 10.1016/j.hemonc.2017.07.002. [Epub ahead of print].
[4] Marsh RA, Allen CE, McClain KL, et al. Salvage therapy of refractory hemophagocytic lymphohistiocytosis with alemtuzumab. Pediatr Blood Cancer 2013;60:101–9.

SP-41
The approach and diagnosis of Coombs negative hemolytic anemias

Achille Iolascon
University of Naples Federico II Naples (Italy)

Anemia affects 1.6 billion of people worldwide, about 10% of these individuals are affected by rare anemias of which 80% are hereditary [1]. Hereditary anemias (HA) embrace a highly heterogeneous group of disorders characterized by anemia of variable degree and by complex genotype-phenotype correlations. Differential diagnosis, classification, and patient stratification among HA are often very difficult.

To date, the major current application of next generation sequencing (NGS) in diagnostics is through disease-targeted tests for which multiple causal genes are known. Some studies have already demonstrated the utility of targeted-NGS (t-NGS) approach in the study of specific subtypes of HA patients. Here, we described the diagnostic workflow based on t-NGS that we developed for the diagnosis of patients affected by HA. Within this wide group of disorders, we included: (1) hyporegenerative anemias, as congenital dyserythropoietic anemias (CDA); (2) hemolytic anemias due to red cell membrane defects, as hereditary spherocytosis (HS) and stomatocytosis (HSt); hemolytic anemias due to enzymatic defects, as pyruvate kinase (PK) deficiency [2–5].

We generated two consecutive versions of the same custom gene panel: the first including 34 genes, the second 71 genes. The probe design was performed by SureDesign (Agilent Technologies, USA). Sample preparation was obtained by HaloPlex Target Enrichment kit for Illumina Sequencing (Agilent Technologies), and high-throughput sequencing was performed by Illumina NextSeq 500. For bioinformatic analyses we used Agilent SureCall software (v 3.0.3.1, Agilent Technologies). The pathogenicity of each variant was evaluated according to the guidelines of ACMG [6,7].

We investigated 74 probands with clinical suspicion of HA. Our approach revealed a diagnostic yield of 64.9% of analysed patients. Genetic data by t-NGS analysis confirmed the clinical suspicion in 54.2% of patients. Of note, most of these patients were originally suspected to suffer from red cell membrane disorders (HSt or HS).

Conversely, t-NGS analysis modified the original diagnosis in 45.8% of patients. Particularly, 81.8% of these patients were clinically suspected to suffer from CDA. Of note, among 22 patients originally classified as CDA, we identified 45.5% of cases with a conclusive genetic diagnosis of congenital hemolytic anemias due to enzymatic defects. Indeed, we diagnosed: (i) one case with biallelic mutations in *GPI*, the causative gene of hemolytic non-spherocytic anemia due to glucose phosphate isomerase deficiency; (ii) another case due to mutations in *AK1* gene, the causative locus of hemolytic anemia due to adenylate kinase deficiency; (iii) eight cases due to mutations in *PKLR*, the causative gene of pyruvate kinase (PK) deficiency [7].

Our observation about congenital hemolytic anemia patients misdiagnosed as CDAs is highly relevant: it underlines how t-NGS analysis is valuable not only for achieving a correct and conclusive diagnosis but also for guiding possible treatment of HA patients. This is mainly true for the treatment of PK deficient-patients, for whom it is now available an allosteric activator of PK enzyme that is able to increase the enzymatic activity in patient erythrocytes treated ex vivo [8].

References

[1] Hertz L, et al. Is increased intracellular calcium in red blood cells a common component in the molecular mechanism causing anemia? Front Physiol 2017;8:673.
[2] Gambale A, et al. Diagnosis and management of congenital dyserythropoietic anemias. Expert Rev Hematol 2016;9(3):283–96.
[3] Andolfo I, et al. New insights on hereditary erythrocyte membrane defects. Haematologica 2016;101(11):1284–94.
[4] Andolfo I, et al. Hereditary stomatocytosis: an underdiagnosed condition. Am J Hematol 2018;93(1):107–21.
[5] Canu G, et al. Red blood cell PK deficiency: an update of PK-LR gene mutation database. Blood Cells Mol Dis 2016;57:100–9.
[6] Al-Riyami AZ, et al. Targeted next generation sequencing identifies a novel β-spectrin gene mutation A2059P in two Omani children with hereditary pyropoikilocytosis. Am J Hematol 2017;92(10):E607–9.
[7] Russo R, et al. Multi-gene panel testing improves diagnosis and management of patients with hereditary anemias. Am J Hematol 2018;93(5):672–82.
[8] Kung C, et al. AG-348 enhances pyruvate kinase activity in red blood cells from patients with pyruvate kinase deficiency. Blood 2017;130(11):1347–56.

SP-42
The nurse and patient partnership in lymphomas

Erik Aerts
University Hospital Zürich, Switzerland

Lymphomas represent the most common form of blood cancer and are divided into Hodgkin lymphoma and Non-Hodgkin lymphomas. They affect all age groups with increasing incidence in older age. The last few years have seen unprecedented advances in highly active novel therapeutic approaches. This exciting new era was heralded by the arrival of anti-CD20 monoclonal antibodies and immuno-chemotherapy which led to improvements in outcome for patients with lymphoma. Despite these advances, relapsed and refractory disease for many patients still represents a major treatment challenge.

Nurses and related health care professionals (HCP) play a major role in the management and delivery of lymphoma treatment for patients and their carers. Continual developments in lymphoma patient management mandates ongoing education of staff working within this field.

Haematology/Oncology nurses require special educational preparation in order to meet the diverse and complex needs of cancer patients and their families throughout the course of their disease.

SP-43
Non-malignant haematological disease (thalassemia, sickle cell) or multiple myeloma)

Erik Aerts
University Hospital Zürich, Switzerland

Managing multiple myeloma: what nurses and healthcare professionals need to know

Aims: To equip nurses with the knowledge needed to monitor and to provide effective management and support to patients with multiple myeloma, with a view to improving treatment adherence and optimizing outcomes.

Implications for nursing: Nurses play a key role in facilitating the management of multiple myeloma throughout the patient journey, providing much-needed support and advice to patients throughout presentation, diagnosis and treatment; they also have a pivotal role in educating patients about treatment options, managing complications during advanced disease stages, and facilitating ongoing communication between patients and the

multidisciplinary team. To succeed in this role, nurses require a thorough understanding of current evidence-based symptom-management programs and a good awareness of the efficacy and safety profiles of newer drugs.

SP-44

Fertility preservation in pediatric oncology and hematopoietic stem cell transplantation

Fatih Erbey
Koç University, İstanbul, Turkey

Nowadays, with the improvements in cancer diagnosis and treatments, life expectancy is prolonged, but this brings some additional problems. After life is saved, the quality of life expectations increase. Healthy sexual life and fertilization are among these expectations.

In oncologic patients, infertility may be directly related to the primary disease, as well as anatomical problems, primary or secondary hormonal insufficiency and germinal stem cell damage may be the cause of infertility. The effects of chemotherapy and radiotherapy on males are decreased sperm count and disrupted morphology, motility and DNA integrity, while decrease in the number of primordial follicles in women, impaired hormonal balance, anatomic-vascular changes and dysfunction of uterus-cervix.

Effects of surgical treatments

Central nervous system (CNS) surgery, especially hypothalamus and/or pituitary surgery, leads to secondary hypogonadism. Primary hypogonadism may develop with direct surgical intervention on ovaries and testes.

Effects of chemotherapy

Although there is no evidence that cytotoxic drugs affect hypothalamus and pituitary function, it is well known that it affects gonads. In the prepubertal period, alkylating agents are the most common cause of azoospermia. While BCNU and CCNU causes prolonged germinal aplasia, drugs such as doxorubicin, ARA-C, and cisplatine may cause mild and reversible gonadal damage. Chemotherapy during this period is not toxic to Leydig cells.

Chemotherapy to prepubertal ovaries is less toxic than postpubertal. During this period, the toxicity due to standard dose alkylating agents is reversible and alkylating agents may delay menarche.

In the postpubertal period, azoospermia, small testicular volume, and decrease in testicular blood flow are reported with chemotherapy. Normospermia may develop within 3 months-3 years due to the effect of stem spermatogonia. The longer the duration of azoospermia, the less chance of recovery. Drugs such as procarbazine, cyclophosphamide, cisplatine, and chlorambucil cause severe stem spermatogonia toxicity and long-term azoospermia.

Decrease in testosterone, increase in LH and gynecomastia may be detected in adolescents due to Leydig cell involvement. LH may increase, testosterone is not affected and, gynecomastia is not seen in adults.

In the postpubertal period, transient amenorrhea develops if maturation follicles are affected and permanent amenorrhea develops if primordial follicles are affected. As the number of follicles decreases with age, chemotherapy in old age causes permanent amenorrhea. Estrogen replacement may be necessary due to ovarian failure and early menopause. The most risky drugs are alkylating agents. The risk increases with age and cumulative dose. Drugs such as cyclophosphamide, busulfan, chlorambucil, mitomycin C, and procarbazine cause ovarian failure and permanent amenorrhea.

Effects of radiotherapy

Secondary hypogonadism due to hypothalamic and/or pituitary damage may develop in CNS radiotherapy. FSH, LH secretion can be suppressed. Delayed or precocious puberty may develop. In adults, dose-dependent FSH, LH are suppressed (oligomenorrhea, testosterone deficiency). Prophylactic cranio radiotherapy may affect the axis but has little effect on gonadotropins.

In the prebubertal period, germ cells are more sensitive to radiotherapy than Leydig cells. Oligospermia, prolonged or persistent azoospermia may develop. Doses above 20 Gy affect Leydig cells and the development of puberty. Testosterone level is very low in affected cases.

Prepubertal ovaries are more radioresistant than postpubertal ovaries. In this period, radiotherapy may lead to dose-dependent ovarian failure, delayed puberty and infertility.

Toxicity in the postpubertal period is related to dose and patient age. Leydig cells are more radioresistant than germ cells in postpubertal period. Permanent azoospermia develops at doses above 2.5 Gy, while oligo-azospermia develops at lower doses. Leydig cell damage develops at doses greater than 30 Gy.

Radiation doses that cause permanent ovarian failure:

20 years old → 5 Gy
35 years old → 3 Gy
45 years old → ≤2 Gy

In women over 40 years, 4-7 Gy radiotherapy leads to irreversible ovarian failure. During total body irradiation (TBI), doses of 8-12 Gy usually result in infertility. Loss of endometrial function, defective implantation, premature and low birth weight deliveries due to radiotherapy have been reported. In those who underwent TBI, the uterus is small and the rate of spontaneous abortion is high.

Preservation of fertility in oncologic treatments

Postpubertal boys

Currently the standard method for postpubertal boys is freezing storage of semen and in-vitro fertilization. If cryopreservation can be achieved, pregnancy can be achieved by intrastoplasmic sperm injection, even with a single active sperm. The likelihood of anomaly and cancer transmission is not different from normal. Semen collection is likely to be feasible in pubertal boys with at least a Tanner III stage and a testicular volume of >6 ml. Younger postpubertal boys who are unable to ejaculate may be offered vibrator stimulation electroejaculation under sedation. Testicular biopsy or sperm aspiration can be performed in postpubertal males who cannot give an example.

Prepubertal boys

Spermatogenesis has not begun in immature boys, and hence the collection of testicular tissue containing spermatogonial stem cells is the only feasible approach for prepubertal boys. Experimentally, prepubertal testicular tissue samples taken before treatment can be frozen and used for future fertilization.

Postpubertal girls

Transvaginal oocyte collection after hormonal ovarian hyperstimulation, followed by cryopreservation, is an established technique in adult females and postpubertal girls. Ovarian tissue cryopreservation is usually considered when oocyte cannot be harvested, often because the restricted time schedule. Ovarian suppression in postpubertal girls by means of gonadotropin-releasing hormone agonists (GnRHa) during chemotherapy may increase the chance of restoring menstrual function and eventually reducing the risk of premature ovarian failure, but no conclusive data have been reported.

Prepubertal girls

Ovarian tissue collection followed by cryopreservation is the only feasible approach to fertility preservation in prepubertal girls. Ovarian tissue in prepubertal girls consists of primordial follicles. The in vitro growth of primordial follicles to mature oocytes has not yet been achieved in humans.

References

[1] Tokuç G, Tokuç R. Pediatrik onkoloji hastalarında fertilite. Pediatrik Onkoloji. 1. Baskı, İstanbul: Nobel Tıp Kitabevleri; 2009: pp. 1399–1405.
[2] Balduzzi A, Dalle J-H, Jahnukainen K, et al. Fertility preservation issues in pediatric hematopoietic stem cell transplantation: practical approaches from the consensus of the Pediatric Diseases Working Party of the EBMT and International BFM Study Group. Bone Marrow Transplant 2017;52:1406–15.
[3] Borgmann-Staudt A, Rendtorff R, Reinmuth S, et al. Fertility after allogeneic haematopoietic stem cell transplantation in childhood and adolescence. Bone Marrow Transplant 2012;47:271–6.
[4] Lambertini M, Del Mastro L, Pescio MC, et al. Cancer and fertility preservation: international recommendations from an expert meeting. BMC Med 2016;14:1.
[5] Chow EJ, Stratton KL, Leisenring WM, et al. Pregnancy after chemotherapy in male and female survivors of childhood cancer treated between 1970 and 1999: a report from the Childhood Cancer Survivor Study cohort. Lancet Oncol 2016;17:567–76.

Oral Presentations

OP-01

Regulatory T cells in peripheral blood and bone marrow in patients with B-cell lymphoproliferative diseases

T. Mushkarına, E. Kuzmına, T. Konstantınova, S. Samborsky
A. Tsyb Medical Radiological Research Center – branch of the National Medical Research Radiological Center of the Ministry of Health of the Russian Federation

Objective: Regulatory T-cells (Treg) is the main population of suppressor cells, which functioning allows the body to avoid the development of autoaggression. These cells are also found in the tumor microenvironment. The increase in their quantity is associated with the decrease in the effector immune response. The study of their functioning in lymphoproliferative diseases is important and priority aspect, which allows to receive new information about the possibility of the regulatory T-cells participation in the mechanisms of immune response suppression in this pathology. Objective of this study - to compare the quantity of regulatory T-cells in primary untreated patients' peripheral blood and bone marrow with two types of B-lymphoproliferative diseases: B-cell chronic lymphocytic leukemia (B-CLL) and diffuse large B-cell lymphoma (DLBCL).
Methodology: The study used the case reports of 78 patients with DLBCL and B-CLL and the data of 56 healthy people. The initial level of regulatory T-cells was analyzed in the peripheral blood of 40 patients with B-CLL and 9 patients with DLBCL, as well as in the bone marrow - 17 and 15 patients, respectively. Neoplastic cells were not detected in the bone marrow and blood of patients with DLBCL. The control group was 40 samples of peripheral blood and 16 samples of bone marrow of healthy donors. Dilution of the bone marrow was excluded according to myelogram data. The detection of Treg CD45+CD4+CD25+CD127low/– was performed by multicolor flow cytometry. Group means are compared using the Student's t-test and the Mann-Whitney U-test at the "STATISTICA 8.0" software.
Results: 1. Regulatory T-cells of healthy donors Treg cells are found in 3.69±1.89% and in the quantity 0.031±0.017×10^9cell/l in the peripheral blood. Treg level in bone marrow are similar to their level in peripheral blood (3.30±1.38% and 0.041±0.023×10^9 cell/l, p>0.05). 2. Regulatory T-cells at DLBCL In untreated patients' with the DLBCL the percentage of regulatory T cells was 5.64± 2.55% in the blood; their level was 1.5 times higher in the bone marrow than in the blood - 8.73±2.55% (p<0.05). The absolute quantity was 0.037±0.03 and 0.19±0.17×10^9 cell/l for blood and bone marrow respectively (p<0.05). Thus, with DLBC in the case of a localized process, the relative and absolute number of Treg cells is increased in the bone marrow, while only their percentage is increased in the blood. 3. Regulatory T-cells at B-CLL. At the B-CLL, the percentage and quantity of regulatory T-cells was 8.15±3.18% and 0.161±0.119×10^9 cell/l in the peripheral blood, that was significantly different from the normal (p<0.05). Their percentage is 11.74±5.07% and the absolute quantity is 0.47±0.42×10^9 cell/l in the bone marrow, which is 1.5 and 3 times higher than their concentration in peripheral blood (p<0.05). In the common form, B-CLL, the percentage and quantity of Treg cells also exceed their levels in DLBCL (p<0.05).
Conclusion: Thus, the increased level of migration of Treg-cells to the bone marrow can be attributed to the predictive signs of the formation of favorable conditions for their delay and the implementation of suppressive action on the populations of cells present in the bone marrow. In the case of B-CLL, the detection of increased amounts of Treg in the bone marrow can occur both due to their more powerful migration, and due to the local transformation of T-helpers into Treg cells, that favor the development and progression of the disease. Finding out the causes of Treg increase in bone marrow and blood, as well as possible mechanisms of their functions realization, should be the subject of further research.

OP-02

The prophylaxis and the treatment of hepatic veno-occlusive disease after pediatric hematopoetic stem cell transplantation: our single-centre experience

B. Karagün[1], B. Antmen[1], İ. Şaşmaz[2], T. Akbaş[3]
[1]Department of Pediatric Hematology/Oncology & Bone Marrow Transplantation Unit, Faculty of Medicine, Acibadem University, Adana Hospital; [2]Department of Pediatric Hematology and Oncology, Faculty of Medicine, Cukurova University, 01130 Adana, Turkey; [3]Department of Radiology, Faculty of Medicine, Acibadem University, Adana Hospital, 01130 Adana, Turkey

Objective: Veno-occlusive disease (VOD) is a leading cause of morbidity and mortality after hemopoietic stem cell transplantation (HSCT).Defibrotide (DF) is considered a safe and effective treatment in VOD. However, patients with VOD have a high mortality rate despite DF use. Preclinical studies have shown that DF has protective effects on activated endothelial cells and it has been suggested that DF can be used prophylactically to benefit from this protective effect. Our aim was to evaluate the efficacy of defibrotide prophylaxis in HSCT recipients at our center.
Methodology: A total of 236 transplants in 210 patients from January 2013 to July 2018 were included in this study. DF prophylaxis (25 mg/kg/day) was given to all patients with factors increasing the risk of VOD. Diagnoses were made via the EBMT 2017 VOD criteria and patients who developed VOD received treatment with increased DF dose (40 mg/kg/day) and supportive interventions. After complete remission of VOD findings, patients were returned to the prophylaxis dose. Close follow-up of patients was performed until 100 days.
Results: In total, 17 patients developed VOD (7.2%). The most common clinical findings were weight increase, hepatomegaly, right upper quadrant pain and ascites development. No adverse events were reported in any of the patients.
Conclusion: Our findings are consistent with previous studies on this topic, and we believe that the use of DF as a prophylactic agent for VOD is beneficial for pediatric patients with risk factors.

OP-03

Is there any impact of uric acid levels during the peri-transplant period on acute graft vs. disease incidence and allotransplant outcome?

P. Kaloyannıdıs[1], H. Alsubaıe[1], R. Omarı[2], S. Kanfar[2], Z. Al Shamması[2], K. Ajlan[3], N. Muhlem[4], A. Lıacını[3], A. Bahranı[5], H. Al Hashmı[2], K. Al Anezı[2]
[1]Adult Hematology & Stem Cell Transplantation Department, King Fahad Specialist Hospital, Dammam, Saudi Arabia; [2]Adult Hematology & Stem Cell Transplantation Department, King Fahad Specialist Hospital, Dammam, Saudi Arabia; [3]Laboratory Technologist Department, King Fahad Specialist Hospital, Dammam, Saudi Arabia; [4]Pathology and Lab Medicine Department, King Fahad Specialist Hospital, Dammam, Saudi Arabia; [5]King Fahad Specialist Hospital, Dammam, Saudi Arabia

Objective: Uric acid (UA), a damage-associated molecular pattern (DAMP) family molecule, upon its release from damaged tissues after the conditioning regimen, activates the alloreactive donor T-cells. Currently, only two published studies evaluated the influence of UA levels at day 0 on the aGvHD occurrence, with totally conflicting results. Given that aGvHD takes place during the whole early post-transplant period, contrasting to previous studies, we evaluated serum UA levels in 4 different time points during the transplant period, at days –7, 0, +7, +14, and investigated its impact on the aGvHD incidence, and the transplant outcome.
Methodology: We retrospectively evaluated 57 patients (pts), with a median age of 36.8 (17-62) years, who underwent allogeneic stem cell transplantation (alloSCT) from full matched sibling donors, either for malignant (n=48) or non-malignant (n =9) hematological diseases. A median of 5.6×10^6/kg CD34+ cells were infused after a myeloablative (n=34) or reduced intensity (n=23) regimen. At the time of alloSCT, 42 pts were in remission (CR1: 30, CR2: 10, >CR2: 2). All pts received either allopurinol or rasburicase from the day of conditioning initiation till day –1. The ROC-curve method, t-test, Kaplan-Meir method, and log-rank test were used for the univariate while the binary logistic regression method for the multivariate statistical analysis. Disease

phase [early (CR1) vs. intermediate (CR2) and advanced (>CR2 or presence of residual disease)], donor gender, patient and donor age, UA levels at day –7, 0, +7, +14, type of conditioning regimens and number of infused CD34+ cells were tested as possible factors that can affect aGvHD incidence.
Results: The median UA levels were 3.2, 2.4, 2.2 and 2.9 mg/dl at days –7, 0, +7 and +14 respectively; the cutoff point was determined at 4.4 mg/dl for day -7 and 2.2 mg/dl for days 0, +7 and +14. Tewnty (35%) pts developed aGvHD; 18(31%) gr ≥II, while 10 (17%) gr III-IV. A higher incidence of aGvHD gr ≥II was noticed for pts with UA levels ≤4.4 mg/dl at day –7 (14 vs 4 pts, p=ns) and for those pts with UA levels ≥2.2 mg/dl at days 0 (12 vs. 6, p=ns) and +14 (13 vs. 5, p=ns). In multivariate analysis, only the number of CD34+ >6×10^6/kg was an adverse factor for aGVHD gr≥II (p=0.04) while intermediate & advanced disease phase along with a number of CD34+ cells >6×10^6/kg, proved to be significant contributors for severe aGvHD (gr III-IV) occurrence (p<0.03). We observed a better 4 years overall survival for pts with UA levels <2.2 mg/dl at day +14 (85% vs. 55%, p=0.06). Fifteen pts succumbed to nonrelapse mortality (NRM) causes; 8/15 deaths were attributed to aGvHD complications. Pts with UA levels ≥2.2 mg/dl at day +14 had higher NRM incidence (p=0.2)
Conclusion: Our results, though not of strong statistical significance, demonstrated that UA levels might affect aGvHD incidence as well as survival and the NRM rates post alloSCT. Definitely, well designed prospective trials are warranted to clarify the role of UA on alloSCT outcome.

OP-04
Relation between fatigue and quality of life in cancer patients receiving outpatient chemotherapy

F. Ipek, V. Yıldız Kabak, S. Atasavun Uysal, T. Duger
Hacettepe University

Objective: The aim of this study was to investigate the relationship between fatigue and quality of life in cancer patients receiving outpatient chemotherapy.
Methodology: Cancer patients receiving outpatient chemotherapy (female:12, male:15) were included in the study. Participants had different cancer diagnoses; breast (n=6), lung (n=3), colon (n=3), pancreatic (n=3) and other cancer (n=12), and their mean age was 56.89±11.08. The fatigue severity of the patients was assessed by the Brief Fatigue Inventory (BFI), and the quality of life was evaluated by The European Organization of Research and Treatment of Cancer Quality of Life Core Questionnaire-C30 (EORTC QLQ-C30).
Results: There was a strong correlation between fatigue and EORTC QLQ C-30 functional scales (r=–0.78, p<0.001). Furthermore, the relationship between fatigue and EORTC QLQ C-30 symptom scale was in moderate correlation (r=0.65, p<0.001).
Conclusion: We found that fatigue in patients receiving outpatient chemotherapy was closely related to quality of life. Interventions to reduce fatigue may help improve the quality of life by increasing the functionality of patients in physical, role, cognitive, emotional and social areas.

OP-05
Secondary AML patients with poor risk cytogenetics have a high risk of death post allogeneic stem cell transplantation in absence of chronic GVHD

M. Hassanein, T. Elhassan, S. Hashmi
King Faisal specialist Hospital

Introduction: Secondary AML (s-AML) includes AML on top of antecedent hematological disorder or therapy related AML. Large registry-based data identified s-AML as an independent poor outcome type of AML post allogeneic stem cell transplantation (allo-SCT). The presence of poor risk cytogenetics in patients with s-AML is a definite indicator of poor survival.
Methodology: A total of 64 patients aged (14–61 years) with s-AML received Allogenic-SCT at our institute. Most of the studied patients were transplanted from a Matched Related Donor (MRD) (54, 84.4%). We retrospectively analyze their data trying to define patients with s-AML, who may truly benefit from Allo-SCT.
Results: Our results showed that poor risk cytogenetics were identified in 31 patients (48.4%) and their presence was a definite indicator of a poor OS and DFS (p=0.009, and 0.004 respectively). The cumulative incidence of chronic GVHD (cGVHD) was significantly lower in s-AML patients with poor risk cytogenetics (p=0.003) resulting in high risk of death without cGVHD in this group of patients (p=0.02). In addition, GRFS analysis showed that most of our studied patients experienced either relapse or debilitating grade II–IV cGVHD in the first 2 years post allo-SCT.
Conclusion: We can conclude that s-AML patients with poor risk cytogenetics have a significantly lower DFS post allo-SCT with a high risk of death without active cGVHD suggesting the lack of benefit from the GVL effect of cellular therapy.

OP-06
Characterization of MAPK signaling pathway in newly diagnosed multiple myeloma

A. Sergeeva[1], V. Surin[2], L. Mendeleeva[2]
[1]National Research Center for Hematology; [2]National Research Center for Hematology

Objective: Multiple myeloma is an incurable plasma cell disease. It is assumed that the pathogenesis of MM is mediated by the hierarchical activation of a number of signaling pathways; one of the key pathway is the mitogen-activated kinase signaling pathway (MAPK cascade). The aim of this study is to characterize MAPK cascade in NDMM. Here we studied the mutation status of RAS genes (k-RAS, n-RAS), BRAF and MAPK gene expression panel and estimated the expression level of MAPK pathway panel genes.
Methodology: We purified CD138+ cells from mononuclear cells using anti-CD138 antibodies according to the Miltenyi Biotec protocol for OctoMacs magnetic separator. We evaluated the resulting fraction with flow cytometry to use it for the genomic DNA and RNA extraction. We analyzed k-RAS, n-RAS (58 patients) and BRAF (23 patients) genes using Sanger sequencing. We also performed gene expression analysis with RNA-seq by Illumina (60 patients). Statistical analysis has been made in STATISTICA.
Results: We analyzed the expression of 198 genes, level of expression of 57 (28.8%) genes is significantly different (criteria Mann-Whitney p<0.005) between donors and MM patients, 15 of genes were upregulated, 42 of them were downregulated. The targets of MAPK pathway – transcriptional factors (TFs) MYC, FOS, JUN were upregulated simultaneously in 2 patients, only MYC and FOS were upregulated in 2 patients, 4 patients MYC and JUN, 26 patients had only MYC upregulated. The downstream targets of these genes – apoptosis inhibitors (BIRC5, MCL-1, BCL-2) - were upregulated in 30 patients, 21 (38.2%) of those ones had higher expression of TFs and apoptosis inhibitors at the same time. There were 14 cases (25.5%) with only TFs upregulation. There were 10 cases (18%) with only apoptosis inhibitors upregulation. We did not see any changes in the target gene expression in 10 patients (18%). We detected RAS mutations in 22 patients (37.9%), the majority of which were found in the activating codons 12, 13, 61, 117, 146. Totally there were 26 RAS mutations detected, 14 out of them were mutations in the n-RAS gene and 12 – in k-RAS gene. There were two mutations in the homozygous state in the k-RAS gene. No BRAF mutations were found. RAS activating mutation(s) and apoptosis inhibitors upregulation were detected in 9 cases (16.4%).
Conclusion: MAPK cascade in NDMM is affected in 90% cases. We could see that 38.2% MAPK pathway contributes to the proliferation as we observed increased level of the target TFs and apoptosis inhibitors. The group which got the upregulated signal from TFs and no changes in apoptosis inhibitors (25.5%) probably has no proliferation signal from MAPK cascade. We concluded that other signaling pathways activated if we got higher expression signal only from apoptosis inhibitors (18%). RAS mutation partially contribute to the myeloma cell proliferation (16.4%).

OP-07

Original versus generic lenalidomide in patients with relapsed multiple myeloma: comparison of effectivity and adverse events

A. Bolaman[1], S. Ertop[2], A. Turgutkaya[1], C. Selim[1], A. Eroglu Kucukerdiler[1], B. Sahip[2], I. Yavasoglu[1]
[1]Adnan Menderes University, School of Medicine, Department of Hematology, Aydin, Turkey; [2]Bulent Ecevit University School of Medicine, Department of Hematology, Zonguldak, Turkey

Objective: Lenalidomide is an effective IMID derivative drug in the treatment of patients with multiple myeloma. Lenalidomide is available as original and generic forms in our country. So far, there is no any clinical study comparing generic and original lenalidomine for effectivity and adverse events. We compared generic and original lenalidomide effects and adverse events (AEs) in patients with relapsed multiple myeloma (RMM).
Methodology: The patients with RMM using original or generic lenalidomide were evaluated as retrospectively. Overall response (OR), complete response (CR), very good partial response (VGPR), partial response (PR), stable disease and progressive disease rates and also for adverse events, development rates of neutropenia, anemia, thrombocytopenia, febrile neutropenia, anorexia, constipation diarrhea, nausea, vomiting, creatinine increase, transaminase increase, asthenia, fatigue, pyrexia, peripheral edema, upper respiratory system infection, pneumonia, another infection, muscle cramp, back pain, bone pain, muscle weakness, arthralgia, headache, tremor, paresthesia, deep vein thrombosis, pulmonary embolism, hyperglycemia, hypokalemia, hypocalcemia, hypomagnesaemia, skin dry and skin erythema were investigated in myeloma patients. All data were analyzed using the PASW for Windows version 19.0 (SPSS Inc., Chicago, IL, USA). The results were described as a number, frequency, and percentage. The chi-squared test and Fisher's exact test were used for the analysis of categorical data and independence between variables. The results were assessed at 95% confidence interval and p-value of less than 0.05 was accepted as significant.
Results: The number of patients using original lenalidomide was 55 and the number of patients using generic lenalidomide was 43. OR rate was 60% versus 39.5% in patients using original and generic lenalidomide significantly, respectively. CR rate was 14.5%, VGPR was rate 45.4% in original group while CR rate was 20.9 and VGPR 18.6 in patients using generic lenalidomide. AEs were usually grade 1 or 2 and they were lower in the original lenalidomide group than in the generic group without significance
Conclusion: Our study showed original and generic forms of lenalidomide are effective for the treatment of RMM. OR rate was higher while in original lenalidomide than generic lenalidomide. The AEs of original lenalidomide were lower than generic lenalidomide without statistically significance. Further studies involving a larger number of patients with RMM would be useful for comparing the efficacy and AEs of original or generic lenalidomide.

OP-08

The efficacy and safety of granulocyte transfusion in pediatric neutropenic patients

G. Akın Kagızmanlı[1], Z. Guzelkucuk[2], P. Isık[2], A. Kara[2], N. Ozbek[2], N. Yaralı[2]
[1]University of Health Sciences, Ankara Child Health and Diseases Hematology Oncology Training and Research Hospital, Department of Pediatrics; [2]University of Health Sciences, Ankara Child Health and Diseases Hematology Oncology Training and Research Hospital, Department of Pediatric Hematology and Oncology

Objective: Intensive chemotherapies and hematopoietic stem cell transplantation suppress bone marrow production and cause severe neutropenia. Bacterial and invasive fungal infections are the major causes of morbidity and mortality in febrile neutropenic patients. Granulocyte transfusion is a logical therapeutic approach as a replacement therapy if infection control cannot be achieved despite effective antimicrobial agents and supportive therapies. The aim of this study was to evaluate the efficacy and safety of granulocyte suspensions in neutropenic pediatric patients.
Methodology: In this retrospective study, 343 granulocyte transfusions applied in 107 febrile neutropenia attacks of 74 patients between 2013 and 2017 were analyzed. The effects of transfusions on hematological and clinical responses and survival were evaluated. Hematological response was defined as an increase in absolute neutrophil counts over 0.5×10^9/L within 24 hours after transfusion and clinical response was defined as normalization of fever within 72 hours after transfusion.
Results: In our study, the mean volume of granulocyte transfusions applied to patients was 237±40 ml. The mean granulocyte counts of the products were $2.8\pm1.3\times10^{10}$/unit. Accordingly, clinical response was achieved in 88 (25.7%) of 343 transfusions. The hematological response was obtained in 163 (47.6%) of 343 transfusions. In 59 (36%) of the granulocyte transfusions both clinical response and hematological response were achieved. Weak correlation between clinical response and hematological response was identified (r=–0.221). The clinical improvement which was defined as the return of the fever to normal within 72 hours and the regression of the signs of infection after the attack, was achieved in 83 (78.5%) of the 107 febrile neutropenia attacks. Granulocyte suspension was generally well tolerated by our patients. Significant side effects were not detected both patients and donors. The cumulative one-month survival rate was 87.8% and the three-month survival rate was 76.5%.
Conclusion: In our study, high hematological response rate was obtained with granulocyte transfusions. Clinical improvement rate and survival rate were also high. These results showed that granulocyte transfusion was effective and reliable. Granulocyte transfusion is a useful treatment approach for immunosuppressive neutropenic patients with severe bacterial and fungal infections that cannot be controlled by broad-spectrum antibacterial/antifungal agents. However, in the therapeutic approach to high risk febrile neutropenia in childhood; well-organized, randomized controlled trials are needed to answer the questions of appropriate dosage, timing and duration of treatment of granulocyte suspension.

OP-09

Thiotepa-based conditioning and autologous stem cell transplantation in children with high-risk medulloblastoma

V. Daylidite, G. Mentkevich, I. Dolgopolov, N. Subbotina, A. Levashov, S. Babelyan, V. Boyarshinov, S. Zagidullina
N. N. Blokhin National Medical Research Centre of Oncology

Objective: Medulloblastoma (MB) is the most common malignant brain tumors in the pediatric population. Despite aggressive treatment including surgery, radiotherapy, and adjuvant chemotherapy, the results in high-risk (HR) patients remains poor. Single or tandem autologous stem cell transplant has been reported to improve outcomes; but optimal conditioning regimen is not well defined. Our strategy is based on combination of thiophosphamide and carboplatin in high dose chemotherapy (HDCT) followed by autologous stem cell transplantation (ASCT) on consolidation stage.
Methodology: 30 patients with HR medulloblastoma who underwent tandem transplant as a consolidation from July 2012 till April 2019 were included. High-risk medulloblastoma was defined by the presence of metastatic disease and/or an incomplete resection with a residual amount of tumor >1.5 cm^2, unfavorable histology type (anaplastic) and/or poor prognosis molecular biology (C myc/N-myc amplification, iso17q). All patients got CT, age-adjusted RT at induction and tandem conditioning with thiotepa 300 mg/m^2 (for pts under 36 months – 10 mg/kg) on days -4, -3 and carboplatin (Carbo) 510 mg/m^2 (for pts under 36 months – 17 mg/kg) on days -4, -3 on consolidation stage followed by autologous stem cell transplantation (ASCT).The median age was 7.4±3.8 years. Regimen toxicity didn't strongly increase after second course. Cumulative organ toxicity was grade two after first course and three - after second. Toxic mortality rate of 6.6% was observed: two patients died of sepsis after second course. One patient died of delayed neurological toxicity (cerebral necrosis) a year after end of treatment. After second course of HDCT 17 patients (56.1%) had no signs of disease, other patients had stable disease without signs of progression. To date 24 patients (79.2%) are alive, one of them relapsed and now is on palliative care, 3 died because of toxicity and 3 patients died after relapse.
Results: We recorded 66.9±11.4% 5-years event-free survival and 67.2±11.7% 5-years disease-free survival in these high-risk group patients.

Conclusion: Tandem transplant in pediatric patients with HRMB is feasible and effective.

OP-10

Role of [^{68}Ga]-pentixafor-PET/CT as a novel imaging of cxcr4 expression in multiple myeloma; comparison to [^{18}F]-FDG-PET/CT

T. Tiryaki[1], S. Kuyumcu[2], D. Has-Şimşek[2], M. Özbalak[1], D. Özlük[1], S. Ünal[2], S. Kalayoğlu-Beşışık[1]
[1]*İstanbul University, Istanbul Medical Faculty, Department of Hematology;*
[2]*İstanbul University, Istanbul Medical Faculty Department of Nuclear Medicine*

Objective: ^{18}F-2-fluoro-2-deoxyglucose (18F-FDG) positron emission tomography/computed tomography (PET/CT) offered the opportunity to precisely stage patients by anatomic and functional techniques in multiple myeloma (MM). [^{18}F]FDG-PET/CT provides also prognostic information on symptomatic MM at the baseline and therapeutic follow-up, allowing the detection of extramedullary disease (EMD). In some cases, [^{18}F]-FDG-PET may be negative due to tumor cell's low glycolytic activity and/or location near the physiologic uptake sites or small in size or patient's low expression of hexokinase-2 gen (catalyzes the first step of glycolysis). PET/CT with a different tracer the CXCR4-directed radiotracer [^{68}Ga]-Pentixafor has also a potential role in MM as being a negative prognostic factor. This study assessed the diagnostic performance of [^{68}Ga]-Pentixafor in MM and aimed also the eligibility for CXCR4-directed radiotherapy.
Methodology: MM patients at diagnosis or relapse referred for [^{18}F]-FDG-PET/CT imaging were evaluated also by [68Ga]-Pentixafor-PET/CT after informed consent. Scans were compared on patients on lesion basis.
Results: Twenty-three MM patients enrolled the study. [^{18}F]-FDG-PET/CT and [^{68}Ga]-Pentixafor-PET were both normal in 6 patients. In the remaining 17 (73%) patients 53 intramedullary lesions were detected on PET/CT images. [^{18}F]-FDG PET showed higher activity in 6 cases and [^{68}Ga]-Pentixafor PET in 9 cases. In 2 patients, both tracer were different for positivity FDG negative lesions were CXCR4 positive and FDG positive lesions were CXCR4 negative mean SUVmax of [^{68}Ga]-Pentixafor-PET/CT was statistically higher compared to [^{18}F]FDG-PET/CT (7.15±5.4 vs 11.1±4.6; p=0.016). In 10 (59%) patients, EMD were detected by both of tracers. However, mean SUVmax of [^{68}Ga]-Pentixafor-PET was significantly higher than [^{18}F]-FDG-PET/CT (9.22 vs 6.55; p<0.05).
Conclusion: CXCR4 expression frequently occurs in advanced MM, representing a negative prognostic factor and a potential target as selecting patients for CXCR4 directed therapies. Our study showed that [^{68}Ga]-Pentixafor-PET/CT is a different novel imaging modality defining the lesions which were negative on FDG/PET. Tumor biology heterogeneity may result different positivity on PET/CT for both of the tracer. [^{68}Ga]-Pentixafor-PET/CT may be more a relevant option in clinical application to follow EMD based on its higher activity compared [^{18}F]-FDG PET/CT.

OP-11

Modern approaches to diagnosis and treatment of various clinical forms of polycythemia vera

F. Khalilova, A. Kerimov, A. Hasanova
Scientific Research Institute of Hematology and Transfusiology

Objective: In recent years clarified that hemoglobin and a hematocrite levels of polycythemia vera (PV) patients can be below the diagnostic criteria of WHO 2008. Hypodiagnosis of PV can lead to decrease in intensity of therapy and worsen efficiency of treatment. Implementation of new diagnostic criterias of PV (WHO of 2016) promotes more accurate definition of clinical forms of a disease and particularly the latent (masked) form of PV.
Case report: The patient, A.I., 1975 date of birth, female, in 12.10.2015 was examined in the city Barda because of the thrombophlebitis of the lower extremities. Due to the changes in a hemoqram she was sent for consultation to the hematologist. In 02.11.15 the patient was examined in Scientific Research Institute of Hematology and Transfusiology. Complaints during receipt were connected with a plethora (an aquagenic itch, a hyperemia of the face, etc.) and a varicose of the right lower extremity (edema in leg, feeling of pain, etc.). The spleen was palpable from under a costal arch for 5 cm. In a hemogram: Hb-150 q/l, RBC 4.8×10^{12}/l, PLT 624×10^{9}/l, WBC 15.4×10^{9}/l, Ht 53.6%. Histological examination of the bone marrow revealed the expansion of all three hematopoietic cell lines. As a result of the molecular and genetic analysis (PCR method) a mutation of JAK2V617F (34.499)was found. A patient was diagnosed with Polycythemia vera. Because of boundary level of hemoglobin, the phlebotomy (FT) was not used as first line therapy. In the course of treatment in steps and depending on the response to treatment the cytostatic-Hydrea, antiaggregants and H2 blockers of histamine receptors were used. Due to the bad tolerance of the Hydrea an administration of this drug was cancelled and treatment continued with an antiaggregant. At the end of the 2016-th year a menometrorrhagia was observed in patient because of the left ovarian cyst. Antiaggregant was cancelled. The patient was several months on treatment and under attendance of the gynecologist. Cases of a menometrorrhagia were suspended, however in connection with the previous bleedings the iron deficiency anemia developed in patient, and the itch even more amplified. An iron therapy and an interferon therapy was appointed. Now the patient feels well. The painful aquagenic itch is not observed.
Methodology: We studied 193 PV patients during the years of 2014-2018. Data are obtained from our institute's databases. Diagnostic methods, a clinical manifestations and treatment methods of patients of PV were analysed. The WHO 2016 classification and the ELN recommendation was used.
Results: Out of 193 patients, 104 were male and 89 were female (1,16:1), median age was 56 (27–87 years). Histological examination of the bone marrow in patients with PV revealed the expansion of all three hematopoietic cell lines. Reticulin fibrosis (MF-1) was determined in 2.9% of patients, MF-2 in 5.7% of patients, in other cases there were no signs of fibrosis (MF-0). The JAK2V617F mutation was detected in 97% of patients; in exon 12 JAK2 mutation was not detected. Average allelic load in JAK2V617F was 41% (3–90%). Cytogenetic studies were performed in 66 patients, abnormalities were detected in 13.7% of patients (del (20q); +8; +9; absence of Y chromosome). The number of patients with thrombotic complications was 22 (11.4%), arterial thrombosis was observed more often than venous. In 6 patients reccurent thrombosis were noted. Out of 193 PV patients, 66 (34.2%) patients were diagnosed with latent form PV and 127 (65.8%) patients with classic form PV. In five years 9 patients (4.7%) transformed to myelofibrosis, 4 patients (2.1%) had a blast transformation of the disease. The latent form of a disease was observed mainly in younger patients. They had lower levels of HGB, RBC, HCT, JAK2V617F allelic load, higher levels of PLT and more often thrombotic complications. Patients received the following types of therapy: a phlebotomy-aspirin – 30 patients (23%), a hydroxycarbamide – 94 (49%),an interferon alfa-2 beta – 27 (14%), a phlebotomy-interferon 7 (3%), a flebotomy -hydroxycarbamide – 21 (10.8%), other – 14 (7.2%). The response to therapy was evaluated according to criteria of ELN 2014. The complete clinical and hematological response was at 52 (26.9%) patients, the partial clinical and hematological response at 121 (62.6%) patients, 20 patients (10.4%) had no response to treatment.
Conclusion: The analysis of PV patients according to the new diagnostic criteria of WHO 2016 allowed to review the diagnosis of PV and to identify latent PV at 1/3 of patients. The most informative way of diagnosis of the latent form of PV is trephine-biopsy of bone marrow. On time diagnosis of the latent form is important for optimization of treatment of PV. However, in general PV has favorable prognosis, decrease in intensity of therapy can lead to increase in frequency of thromboses.

OP-12

Spectrum and geographical distribution of beta-thalassemia mutations in Azerbaijan

G. Aliyeva, C. Asadov, T. Mammadova, S. Gafarova, Y. Guliyeva
Institute of Hematology and Blood Transfusion

Objective: With the carrier rate of 4–8.6%, β-thalassemia is one of the most prevalent hereditary disorders in Azerbaijan. Taking in consideration the high frequency of β-thalassemia as well as the occurrences of several other hemoglobinopathies, we conducted a large genotyping study to investigate the spectrum, geographical distribution and ethnic association of β-thalassemia mutations in Azerbaijanian population.

Methodology: Samples were recruited through population screening (n=1413). The information on the geographical origin was collected, and patients were allocated into 10 groups of geographical regions (Absheron, Ganja-Qazakh, Shaki-Zaqatala, Lankaran, Guba-Khachmaz, Aran, Mountainous Shirvan, Karabakh, Nakhchivan, and Western Azerbaijanians). All the samples allocated to the respective groups were originated from these regions for at least last two generations; samples with mixed origins were excluded. Samples were genotyped via two-step algorithm including reverse dot-blot hybridization and sequencing of HBB gene.
Results: Genotyping of β-thalassemia carriers identified through population screening revealed 35 mutations, with codon 8 [-AA] – 34.96%, IVS-II-1 [G>A] – 16.35%, and IVS-I-110 [G>A] – 10.12% leading the spectrum. Majority of the identified mutations were related to Mediterranean, Middle East, Arabian, Turkish and Kurdish origins. Analysis of the contingency table revealed a significant association of several mutations with certain regions (ri>2.00; p<0.05). The strongest association was observed between codon 8 [-AA] and Shaki-Zaqatala, and codon 5 [-CT] with Mountainous Shirvan regions (ri>6.00). Although codon 8 [-AA] is the most common mutation among the local population, observations did not exceed expected results and it accounted for approximately 35% of the spectrum in the rest regions of the country. The most deviations from expected results was observed in Lankaran region, with IVS-II-1 [G>A], codon 36/37 [-T], codon 14 [+T], codon 5 [-CT], -88 [C>A], -92 [C>T] and codon 44 [-C] mutations showing a significant association. However, the association of the mutations with the lowest observations should be interpreted with caution. Among the mutations with more than 30 observations, significant association was observed in people originated from Karabakh region and codons 82/83 [-G] and codons 8/9 [+G] mutations; Guba-Khachmaz with IVS-I-6 [T>C]; Aran with codon 39 [C>T]; and Mountainous Shirvan with codons 36/37 [-T] and codon 44 [-C] mutations.
Conclusion: Our results allows a better understanding of the wide spectrum of mutations in Azerbaijan and highlights the high heterogeneity of hemoglobinopathies in the local population.

OP-13
Cancer stem cells (CSCs)

Svetlana V. Chulkova
Department of Oncology and Radiation Therapy, Department of Immunology Haematopoiesis of FGBU "NMRC of Oncology named NN Blokhin" of the Ministry of Health of the Russian Federation

All malignant tumors are a heterogeneous population of cells with different biological properties. One of the theories explaining tumor heterogeneity is the theory of tumor stem cells. Small subpopulation of the cancer cells with tumor-initiating capability is the core origin of the tumorigenesis and the subset of cancer cells are named cancer stem cells.
Characteristics and dynamics of CSCs: CSCs have the ability to self-renew and differentiate, as well as stimulate the growth and metastasis of tumors, while most tumor cells have limited proliferative potential. Compared with the dominant clone of tumor cells and normal stem cells, CSCs have dysregulated signaling pathways *(Notch, Hedgehog, Wnt)* and aberrant phenotypes (in breast cancer *CD44+CD24–/low/Lin–*, in leukemia *CD34+CD38–*, in ovarian cancer *CD44+CD117+).* It is important that CSCs require their CSC niches to maintain stem cell properties. The most studied niches are perivascular and hypoxic niches, but other microenvironments composed of various stromal cells have been identified.
A capability for the dynamic transitions (switching of CSCs between epithelial-like and mesenchymal-like states) leads CSCs to adapt to environmental changes in the process of invasion and metastasis thereby affecting tumor progression and imparting therapeutic resistance.
Therapeutic strategy: CSCs harbor endogenous resistance mechanisms against radiation and chemotherapy which gives CSCs a survival advantage over differentiated counterparts. According to recent findings, targeted elimination of pre-existing cancer stem cells is the most promising therapeutic strategy. However, there are limitations of CSC targeting strategies. Seven CSC surface markers are ubiquitously expressed on normal tissue cells, which may lead to side effects when they are targeted for elimination. Also, CSC marker-negative or differentiation marker-positive cancer cells could initiate tumor formation: such as CD271– or CD271+ populations in melanoma. Single cell transcriptome analysis revealed that the cells positive for the different CSC markers or the cells harboring activation of the distinct CSC-specific signaling nodes, could co-exist within a population of tumor cells, and many CSC or cancer subtype markers can be expressed by a cell at the same time. Also, activation of CSC-specific signaling pathways could be different within a tumor, implying that abrogation of a single pathway may not critically affect whole CSCs.
Future: The rapid and repetitive reprogramming process generates a hierarchical organization and a mixed composition of phenotypically distinct subclones. Importantly, each subtype may require activations of distinct and specific signaling pathways, because they show their specific gene expression patterns. Therefore, it is plausible that identifying transcription factor and epigenetic modifier networks involving in CSCs and reprogramming process would be a potential approach to developing CSC targeting strategy.

OP-14
Single institution experience of thymoma and thymic carcinoma patients

M. Sımsek [1], M. Bılıcı [2], S. Tekın [2]
[1]*Yozgat City Hospital;* [2]*Ataturk University*

Objective: Thymoma and thymic carcinoma are rare and very heterogeneous neoplasms. They constitute half of the anterior mediastinal masses being the most common tumors of mediasten in adults. Their clinical course varies from an indolent slow process to a very progressive and metastasizing one. Complete surgical resection is the only curative treatment option for thymic malignancies and recommended to be the gold standard method. Although combined chemotherapy regimens seem to be effective in thymoma, thymic carcinomas have a low response to chemotherapy. In this study, we aimed to evaluate retrospectively the patients diagnosed with thymic malignancies referred to our clinic.
Methodology: We planned to analyze the data of patients diagnosed with thymic malignancies between January 2000 and June 2018. 22 patients with thymic malignancies who admitted to our clinic were included in our study. Data were collected from patient files, digital data processing system, and government death notification system.
Results: Median age was 56 for thymic carcinoma patients. One patient with stage 2 disease is still alive at her tenth year of diagnosis after receiving three lines of chemotherapy. Two patients with stage 3 disease are still alive after treatment with overall survivals over two years. All patients with stage 4 disease were died. Overall survival of these patients ranged from 13 months to 51 months. Median age was 55 for the patients diagnosed with thymoma. One patient with stage 1 disease has undergone surgery without receiving any adjuvant therapy and is still alive at her fifth year of diagnosis. One patient with stage 2 disease had an overall survival of 57 months. Other patient with stage 2 disease did not receive any adjuvant treatments after surgery, and he is still alive after 36 months of diagnosis. For stage 3 disease, overall survival ranged between eighteen months to seven years.
Conclusion: We aimed to share our findings of our patients with thymic malignancy diagnosis. Although patient numbers did not seem to be adequate, we believe that our study will contribute to the literature. In the future, collection of data from different centers and various clinical trials, there will be new approaches to TC and thymoma patients leading to better outcomes.

OP-15

Analysis of the progression-free survival of CLL patients who received first-line bendamustine-rituximab therapy depending on the elimination rate of the minimum residual disease and mutational status IGHV genes

I. Miroliubova, E. Stadnik, V. Strugov, Y. Virz, T. Nikulina, E. Tolstopiatova, A. Rumyantsev, T. Chatalava, N. Timofeeva, A. Zaritskey
Institute of Hematology, Almazov National Medical Research Centre

Objective: It has been proven that residual disease (MRD) status and mutational status of IGHV genes are predictors of the overall and progress-free survival (PFS) in CLL patients who receive chemotherapy and immuno-chemotherapy. According to published data, patients who have achieved MRD-negative status after the first 3 courses of chemotherapy have durable PFS and may not need to continue therapy. In this study, PFS was analyzed in relation to the level of MRD and mutational status of the patients after the 3rd and 6th course of the standard bendamustine-rituximab (BR) regimen in the first line of therapy

Methodology: From 2012 to 2015, the study included 202 patients with a verified diagnosis of CLL and the presence of indications for initiating therapy according to the recommendations of iwCLL (Hallek et al., 2008). The level of MRD of the patients with a complete or partial response was determined after 3 and after 6 courses of therapy. All patients underwent standard BR chemotherapy: (rituximab 375 mg/m^2 to 500 mg/m^2 × 1 day, bendamustine 90 mg/m^2 × 2 days, 6 courses of 28 days). MRD was measured in bone marrow by 4-color flow cytometry according to Rawstron et al., 2007. The mutational status of IGHV genes was determined using the Sanger sequencing method. Statistical analysis was performed using IBM SPSS software, version 21. Survival curves were calculated using the method of Kaplan and Meier, and univariable comparisons were made using the log-rank test. PFS was defined as time from start of treatment to progression or death. All P values were considered significant if p≤0.05.

Results: Data on MRD after 3 courses were obtained from 139 patients. After 3 courses, 15 patients (11%) achieved MRD negativity. After 6 courses, MRD data were obtained from 127 patients, of which 40 were MRD-negative (31.5%). In the analysis of PFS, significantly better rates were among patients who achieved complete eradication of MRD after 3 courses of therapy, in contrast to patients with persistent MRD, regardless of the level of residual tumor clone. Data on MRD and mutational status were obtained from 115 patients. A group of patients with mutated status of IGHV genes who achieved MRD-negativity did not have adverse events during the observation period, regardless of the time period for achieving MRD negativity.

Conclusion: The most durable PFS was found in patients with complete and partial remission who achieved MRD-negativity after 3 courses of therapy and also patients with a mutated status of IGHV genes, who achieved MRD-negative both after 3 and after 6 courses of therapy. Obtained data may be a prerequisite for clinical recommendations for determining MRD after 3 courses in order to individualize therapy.

OP-16

Prognostic implication of Notch 1 expression among adult patients with normal cytogenetic acute myeloid leukaemia

G. Elyamany[1], S. Alotaıbı[2], O. Alsuhaıbanı[1], H. Aljasem[2], A. Mansoor[1]
[1]*Department of Central Military Laboratory and Blood Bank, Prince Sultan Military Medical City (PSMMC), Riyadh, SA;* [2]*Department of Hematopoietic Stem Cell Transplantation and Adult Clinical Hematology, Prince Sultan Military Medical City, Riyadh, SA*

Objective: The majority of AML patients initially respond to current routine induction therapy with complete remission; however, approximately two-third patients discern relapse with poor prognosis. The conventional risk stratification criteria based on cytogenetic abnormalities divide AML patients into three defined risk groups, favourable, intermediate, and unfavourable. AML patients with normal cytogenetics (intermediate-risk) characterises a large and heterogeneous patient group with variable response to conventional therapy and clinical outcome. Improved insight into the biology of AML, especially with normal cytogenetic is warranted to explore new therapeutic targets. Notch 1 is now established to play a key role in the prognosis of several hematological malignancies, however, its role in AML remains controversial. In this pilot study, we correlated Notch1 and associated pathway expression patterns with hematological data and overall survival (OS) among adult AML patients with normal cytogenetics.

Methodology: This pilot study utilized paraffin embedded (FFPE) diagnostic bone marrow (BM) biopsy samples (N=36) from AML patients with normal karyotype. RNA from diagnostic BM biopsies was subjected to expression analysis employing nCounter Pan-Cancer pathway panel by Nanostring technologies. Laboratory and clinical data were correlated with expression of Notch1 and associated molecules.

Results: 36 AML patients (median age 56 yrs., range 18–66 yrs.) were dichotomized into low Notch1 (13/36; 37%) and high Notch1 (23/36;63%) groups based on ROC curve analysis (72% AUC; 93% sensitivity /55% specificity). Age, gender, hematological data or molecular risk factors exposed no significant differences across these two distinct groups. Distribution of FLT3/NPM1 mutation across low Notch1 expression group (23%/62%) versus high Notch1 expression group (48% /65%) was statistically insignificant (p<0.483 and p<0.999). The ROC curve for Notch1, Notch2, Notch3, Notch 4 gene expression analysis revealed that only Notch1 expression show significant association with OS. The dichotomization scheme identified 13/36 (37%) patients in low Notch1 expression group while 23/36 (63%) in high Notch1 expression group. After a median follow-up of 22 months, patients with high Notch1 expression experienced high mortality (13/23; 57%) compared to patients with low Notch1 expression (1/13; 8%) (p<0.0048). Overall, low Notch1 expressers showed better OS (740 days) compared to high Notch1 expressers (579 days) log rank test p<0.023; HR 7.54 (0.98-54.1). High expression of Notch1 correlated with Wnt signaling pathway modulator- Secreted-frizzled related protein 4 (SFRP-4) (>2.0 fold; p<0.001) and several genes associated with micro-environment like Angiopoietins (ANGPTs), Osteopontin (SPP1), bone sialoprotein- IBSP, MMP-9 (>2.0 fold; p<0.001) Our pilot study identified lower level of Kruppel-like factor 4 (KLF4) expression with high Notch1 expression in this cohort with median differential expression of 2-fold.

Conclusion: Our pilot study identified high Notch1 expression as an important poor prognostic marker among AML patients with normal cytogenetics. it appears that Notch proteins are multifaceted and involved in several key cellular functions with extensive crosstalk with other critical pathways which may be deregulated in cancer. High Notch1 expression is associated with poor prognosis. Notch1 expression is independent of conventional risk parameters and can be a potential therapeutic target.

OP-17

Genetic variations in tumor necrosis factor-related apoptosis-inducing ligand receptor 1 (TRAIL-R1) gene and the susceptibility to B cell non-Hodgkin lymphoma in Egypt

M. Khorshied[1], N. Soliman[1], S. Bakr[2], O. Khorshied[1]
[1]*Cairo University, Egypt;* [2]*Fayoum University*

Objective: Apoptosis is essential for normal tissue homeostasis, cellular differentiation and development. Inhibition or blockade of Tumor Necrosis Factor-Related Apoptosis-Inducing Ligand-Receptor 1(TRAIL-R1) may alter its apoptotic function, and subsequently provide growth advantage to neoplastic cells. Genetic polymorphisms in TRAIL-R1 gene has been associated with many cancers.

Aim: To clarify the association between TRAIL-R1 -A1322G, -C626G and -A683C single nucleotide polymorphisms (SNPs) and B-NHL risk in Egyptians.

Methodology: Genotyping of TRAIL-R1 -C626G, -A683C and -A683C SNPs was performed for 100 newly diagnosed, adults, Egyptians B-NHL patients and 150 age and gender matched healthy Egyptian controls.

Results: The frequency of the polymorphic alleles of -C626G and -A1322G were significantly higher in B-NHL patients compared to controls with almost twofold increased risk of B-NHL (OR=1.76; 95% CI=1.01–3.08 and OR=2.1; 95% CI=1.61–3.74 respectively), while there was no statistical difference in the distribution of -A683C polymorphic allele between B-NHL patients and

controls (OR=1; 95% CI=0.5–2). Combined genotypes analysis revealed that coinheritance of the polymorphic genotypes of TRAIL-R1-C626G and -A1322G SNPs was associated with almost three folds increased risk of B-NHL, while coinheritance of the variant genotypes of -A683C and -A1322G SNPs or those of the three studied SNPs was not.

Conclusion: TRAIL-R1–C626G and -A1322G polymorphisms could be considered as molecular risk factors for B-NHL in Egyptian population. Furthermore, the growing interest in TRAIL-based interventions has led to the development of recombinant human TRAIL (rhTRAIL) as a promising target therapy. Accordingly, screening for TRAIL-R1 gene polymorphisms is mandatory for selecting patients who will gain benefit from this novel therapeutic modality

OP-18

Pegylated interferon alfa-2a is effective and decreases LDH levels in patients with essential thrombocythemia and polycythemia vera

O. Ekinci

Firat University, Faculty of Medicine, Department of Hematology

Objective: Pegylated forms of interferon have a better pharmacologic profile than short-acting interferons, resulting in a more convenient less-frequent schedule of injections, less immunogenicity and possibly less toxicity. Also it has been previously reported that pegylated interferon alpha-2a (PEG-IFN-2a) can induce hematologic and molecular responses in patients with essential thrombocythemia (ET) and polycythemia vera (PV). Lactate dehydrogenase (LDH) has been shown as a negative prognostic biomarker for myeloproliferative diseases in several studies. Here we evaluated the efficacy of PEG-IFN-2a and after treatment LDH levels in our patients with ET and PV.

Methodology: Patients that had a diagnosis of ET or PV according to WHO 2016 criteria and received PEG-IFN-2a treatment were included in this retrospective study. All patients received 90 µg per week in the first 2 weeks and then continued with 180 µg per week. Patients' previous treatments, spleen sizes, LDH levels, hemogram parameters and adverse events were identified. SPSS 22.0 was used for statistical analyses. Paired sample T test was used to compare LDH levels before and after treatment.

Results: Forty-one patients were included in this study. Median age was 52 (23–81). Twenty-three patients were male and 18 were female. There were 17 PV patients and 24 ET patients. JAK-2 was positive in 18 patients. Thirty patients were evaluated with bone marrow biopsy and there were grade 0 fibrosis in 1 patient, grade 1 in 19 patients, grade 2 in 7 patients and grade 3 in 3 patients. Median treatment duration for PEG-IFN-2a was 16 months (1–17). Six patients (14%) did not respond to treatment and two patients (5%) could not tolerate PEG-IFN-2a. LDH levels were increased before PEG-IFN-2a treatment in 19 patients. There was a statistically significant decrease in 9th month LDH levels compare to initial levels (p=0.007).In ET patients there was a statistically significant decrease in platelet counts from third month of PEG-IFN-2a (p=0.013). Only one PV patient did not respond to treatment, all others did not need phlebotomy or any other treatment anymore. No thrombotic or hemorrhagic event was seen. Side effects were seen in 11 (26%) patients. Most frequent side effects were fever and weight loss. There was no reduction in spleen size during the follow up period. As of the moment 33 (81%) patients are still on treatment.

Conclusion: PEG-IFN-2a was well tolerated in our study, even elderly patients resumed the therapy. Overall response rate was 86%. Specially PV patients respond well. Hematologic response rate was consistent with studies in the literature but toxicity and side effects were significantly lower in our study group. Although the follow up time was short it is good not to see any thrombotic or hemorrhagic event. We demonstrated a statistically significant decrease in LDH levels. To the best of our knowledge, our study is the first that demonstrates LDH decrease with PEG-IFN-2a. We could not evaluate molecular response yet. PEG-IFN-2a is a great nonleukemogenic option with the chance of molecular remission for PV and ET patients who were resistant or refractory to previous therapies.

OP-19

Two-year experience of a multidisciplinary approach for pediatric thrombosis in a tertiary referral center

Z. Karakas[1], R. Tuna[1], N. Aydinli[2], S. Sencer[3], S. Karaman[1], D. Tugcu[1], A. Unuvar[1], O. Durmaz[4], A. Nayır[5], K. Nisli[6], A. Dindar[6], R. Omeroglu[7], F. Darendeliler[8], Z. Bayramoglu[9], S. Ocak[1]

[1]Istanbul University Faculty of Medicine, Departments of Pediatric Hematology Oncology; [2]Istanbul University Faculty of Medicine, Department of Pediatric Neurology; [3]Istanbul University Faculty of Medicine, Departments of Neuroradiology; [4]Istanbul University Faculty of Medicine, Departments of Pediatric Gastroenterology; [5]Istanbul University Faculty of Medicine, Departments of Pediatric Nephrology; [6]Istanbul University Faculty of Medicine, Departments of Pediatric Cardiology; [7]Istanbul University Faculty of Medicine, Departments of Pediatric Cardiology and Rheumatology; [8]Istanbul University Faculty of Medicine, Departments of Pediatric Endocrinology; [9]Istanbul University Faculty of Medicine, Departments of Pediatric Radiology

Objective: Pediatric thrombosis has unique characteristics due to its epidemiology, pathophysiology and treatment considerations. Children diagnosed with thrombosis have to be evaluated by multidisciplinary team at the level of diagnosis, treatment and follow-up. Here we present our 2-year experience of pediatric thrombosis patients with a multidisciplinary thrombosis council management.

Methodology: Pediatric thrombosis cases were evaluated in a monthly council of pediatric hematology-oncology, pediatric radiology and neuroradyology in addition to other pediatric subspecialities in Istanbul University, Faculty of Medicine. We retrospectively reviewed case presentations and recommendations of the council for 61 children (95 admissions) between November 2017 and August 2019.

Results: Male/female ratio was 1.54 of evaluated 61 patients. Twenty-two patients we reevaluated at follow-up for treatment management or reporting outcome. Five of the patients were newborns,10 were infants, 23 were children (2 to 12 years), 22 were adolescents (12 to 18 years) and 2 were young adults (22 and 26 years, respectively) at diagnosis. All patients were re-evaluated by the radiologist at the multidisciplinary council for primary diagnosis or ongoing management. The diagnosis of the patients was mainly brain thrombosis (arterial: 36%, sinovenous: 32%), others were portal vein thrombosis (6%), renal vein thrombosis (6.5%), deep vein thrombosis (6.5%), cardiac thrombosis (5%), hepatic vein thrombosis (3%), recurrent catheter thrombosis (3%), peripheral artery thrombosis (3%) and pulmonary embolism (1.5%). Six patients were evaluated for anticoagulation prophylaxis without personal history of previous thrombosis; 5 for pre-HRT evaluation and 1 for strong family history, respectively. Concomitant diseases were infection (27%), rheumatologic disease (10%), catheterization (10%), trauma (10%), congenital heart disease (8%), kidney disease (6.5%), malignancy (5%), hemoglobinopathy (3%) and dehydration (3%). Underlying thrombophilia factors were evaluated as high Factor VIII (27%), high homocysteine (23%), Factor V Leiden mutation (16%), protein S deficiency (13%), protein C deficiency (10%), hyperlipidemia (10%), Prothrombin 20210A mutation (6.5%) and Antithrombin III deficiency(6,5%). On the basis of patients' clinical and radiological status, treatment and prophylaxis periods were determined. Thirty-nine patients(64%) received primary or secondary prophylaxis with vitamin K antagonists, aspirin or LMVH for different periods of time.

Conclusion: Cerebral arterial and sinovenous thrombosis were more common in our pediatric thrombosis council cases. It is because pediatricians face more difficulties in the treatment of cerebral thrombosis and our center is a tertiary referral center where complicated cases were referred. Acquired risk factors for thrombosis were more common than congenital ones, infection and elevated Factor VIII were commonest, respectively.

OP-20

The significance of geriatric assessment in elderly patients with B-cell non-Hodgkin lymphoma: a single-centre experience

Z. Cvetkovıc[1], A. Novkovıc[2], Z. Djumıc[2], T. Bıbıc[2], A. Ivanovıc[2]
[1]Medical Faculty University of Belgrade, Belgrade, Serbia, Department of Haematology Clinical Hospital Centre Zemun, Belgrade, Serbia; [2]Department of Haematology Clinical Hospital Centre Zemun, Belgrade, Serbia

Objective: Current prognostic indices for different types of B-cell non-Hodgkin lymphoma (B-NHL) include only age and Eastern Cooperative Oncology Group performance scale (PS) besides disease related parameters. PS is found not effective predictor in the elderly. Comorbidity and functional status are important factors in determining therapy. In aim to avoid suboptimal treatment of elderly cancer patients, it is proposed that all cancer patients ≥65 years of age should undergo a screening assessment for age-dependent functional impairment using screening tools such as G8 questionnaire, together with instruments for determining dependency (IADL - Instrumantal Activities of Daily Living), cognition (MMSE- Mini-Mental State Examination), and comorbidities (CCI-Charlson comorbidity index). As the incidence of B-NHL increases with age, and as the proportion of elderly individuals increases, the individualized treatment approach based on geriatric assessment (GA) should be implemented in routine hematological clinical practice. The objective of the study was to evaluate the impact of GA on clinical outcome and survival of elderly patients with indolent B-NHL.
Methodology: GA was performed in 49 consecutive elderly patients (16 males and 33 females with median age at diagnosis 72,1 years, range 65–85 years) with B-NHL (20 pts with indolent B-NHL who fulfilled criteria for treatment initiation and 29 pts with aggressive B-NHL) diagnosed and treated since January 2014. Patients were treated with antracycline, fludarabine or alkylated agents based chemotherapy regimens ± monoclonal anti-CD20 antibody. Validity of GA was compared with standard relevant clinical and laboratory parameters.
Results: For all 49 patients median overall survival (OS) was 48 months, and disease free survival (DFS) in 39 (79.5%) patients achieving remission was 17 months. Among laboratory parameters, elevated lactate dehydrogense (LDH), β-2 microglobuline (β2M), were found significant for predicting OS, and low platelets count (<100×10^9/L) for CR rate. None of evaluated parameters (hemoglobin, neutrophil count and platelet count, LDH, total protein, albumin and β2M had influence on DFS. Among clinical parameters the presence of "B" symptoms, splenomegaly (>13 cm), bulky disease (BD >10 cm), extranodal (EN) disease, as well age adjusted CCI (aaCCI; <5/≥6), PS (<2/≥2), G8 screening tool (>14/≤14), IADL (0–2/3–5/≥6) and MMSE (<24) were evaluated. BD, G8, IADL and aaCCI were found significant for OS rate; BD and EN for CR rate, and splenomegaly and EN for DFS. BD, IADL and aaCCI confirmed significant in multivariate analysis for OS.
Conclusion: According to our experience, G8 screening tool and IADL are easy to perform and valuable instruments in determining therapy and for predicting survival of elderly B-NHL patients.

OP-21

The incidence and clinical impact of endocrine incidentalomas in hematologic malignancies: a single-center experience

S. Turgut, E. Erdoğan
Bezmialem Vakif University

Objective: Endocrine glands are one of the most frequent organs that incidentally lesions were detected. Incidentalomas of the hypophysis, thyroid, parathyroid, and adrenal, with variable implications, is increasingly seen due to the frequent use of imaging methods in clinical practice. Positron Emission Tomography - Computed Tomography (PET-CT) is a well-established whole-body imaging technique in hematologic malignancy due to staging, treatment planning, monitoring, and frequently identifies incidentalomas. In this study, we aimed to determine the frequency and clinical importance of endocrine incidentalomas detected by PET-CT, and discuss clinical awareness of physicians in approaching these patients who have hematological malignancy.
Methodology: 802 patients (470 lymphoma/332 multiple myeloma) who were admitted to Bezmialem Vakif University Hospital hematology outpatient clinic with the diagnosis of lymphoma and multiple myeloma (MM) between 2012 and 2019 were retrospectively analyzed. The initial PET-CTs of the patients were evaluated. FDG uptake density, SUVmax values, localization, size and number of FDG positive incidentalomas detected in the pituitary, thyroid, parathyroid, and adrenal glands were recorded. Patients with FDG involvement due to primary malignancy were not included in this cross-sectional descriptive study. Interim evaluation and/or post-treatment PET-CT of the patients included in the study were assessed. Hormone profiles, additional imaging, biopsy or operation histories of the patients were investigated according to the detected incidentaloma.
Results: Endocrine incidentalomas were detected in 32 (4%) of 802 patients (13 MM/19 lymphoma). Two patients had pituitary, 24 patients (16 females/8 males) had thyroid, and 6 patients (3 females/3 males) had adrenal incidentaloma. No parathyroid lesion was detected. Two patients of pituitary incidentaloma (mean SUVmax = 12.3±0.4) had MM. Among thyroid incidentalomas (mean SUVmax = 5.3±2.5), 10 were detected in MM patients, 11 were in Non-Hodgkin lymphomas (NHL) and 3 were in Hodgkin lymphomas (HL). Adrenal incidentalomas (mean SUVmax = 7.8±6.5) were detected in one of MM and HL patients and 4 of NHL patients. While 21 patients underwent hormone assessment and 17 patients underwent an ultrasound examination, pituitary and adrenal incidentalomas were not examined further. Five of the thyroid incidentalomas underwent fine-needle aspiration biopsy and 3 patients underwent total thyroidectomy without biopsy for multinodular goiter. Two patients with toxic adenomas were followed up with medical treatment because they were not suitable for curative options. All of the patients who underwent biopsy or surgery had benign pathologies.
Conclusion: This study provides a brief overview of the frequency, clinical impact, and approach to the diagnosis of incidentally discovered endocrine lesions in patients with hematological malignancies by PET-CT in a single center. Endocrine incidentalomas detected especially in malignancies may escape the attention of physicians due to lacking experiences about the necessity of further assessments. Further investigation for these incidentalomas could be playing a crucial role to detect a second malignancy or functional adenomas and contribute to the survival and control comorbidities of the patients. Larger and multicenter studies are needed.

OP-22

Clinical relevance of minor histocompatibility antigens

F. Savran Oguz[1], C. Kekik Cinar[1], S. Oguz[2], D. Sargin[3], S. Kalayoglu Besisik[4]
[1]Istanbul University, Istanbul Faculty of Medicine, Department of Medical Biology, Tissue typing Laboratory, Istanbul; [2]Istanbul Demiroglu Bilim University, Department of Medical Biology, GFN Tissue Typing and Immunogenetic Laboratory, Istanbul; [3]Medipol University, Faculty of Medicine, Department of Hematology, Istanbul; [4]Istanbul University, Istanbul Faculty of Medicine, Department of Hematology, Istanbul

Objective: The minor histocompatibility antigens (MiHA) are epitopes composed of polymorphic essential peptides evoking alloimmune responses limited to a variety of human leukocyte antigen (HLA) alleles. These peptides are allelic cellular proteins and encoded by autosomal genes or by genes of the Y chromosome. MiHAs may be immunogenic or nonimmunogenic in characteristic. They are either ubiquitously expressed in many cells and tissues or restricted to the hematopoietic system cells. Some of these MiHA can also be expressed by tumor cells. Upon hematopoietic stem cell transplantation (HSCT) for hematological malignancies responses to MiHA may develop as graft-versus-host-disease or graft rejection, but can also contribute to the eradication of the tumor cells named graft-versus.-leukemia effect. Our aim was to determine the MiHA distribution in Turkish healthy population and in patients with hematopoietic malignancies whereas some of them were genotypically identical HSCT recipient/donor pair.
Methodology: MiHA data were obtained from 200 healthy individuals, 150 patients with hematopoietic malignancies and 20 HLA genotypically identical HSCT recipient/donor pairs. The study cohort donor–recipient pairs were

selected on the basis of the presence of HLA-A2, which is the HLA restriction molecule for miHA HA-1. MiHA alleles were analysed using the PCR-SSP.

Results: Among 200 healthy individuals, 45.7% had HA-1H allele and 54.2% the HA-1 R allele matching according to Hardy-Weinberg Equilibrium (HWE). Allelic variant genotype distribution in healthy population was as follows; RR with 26.5%, HH with 8% and HR with 55.5%. Among individuals with hematopoietic malignancies, the allelic frequency was for H 43.3%, and for R allele 56.6% which was not different in recipients/donor pairs. Allelic variant genotype distribution was for RR 35%, for HH 10% and for HR 55%. Ten patients were MiHA incompatibile and 50% of them developed aGVHD.

Conclusion: MiHA distribution in Turkish population as a mixed ethnic Asian European population was found to be similar to the other populations. However, the study conducted by Kotzampasaki et al. from Greece, with 49 healthy bone marrow donors revealed the HA-1H, and HA-1R in a frequency of 29%, and 70%, respectively. Goulmy et al. found the HA-1H, and HA-1R as 47.6%, 52.4% in Asian/Pasific islanders, as 47.8%, and 52.2% in the black population, and as 35.9%, 64.1% in white population. This study included a large study cohort as 2262 individuals with 10 different MiHA genotyping from 16 countries, and in 6 different ethnic groups in 5 different continents. MiHA frequency n healthy Turkish population based on our study seemed to be not different from other countries. İn addition to MHAs, MiHA identification may determine the immune response type which may be predictive for the clinical outcome. As a target for posttransplant T-cell immunotherapy.

OP-23

Feasibility of the Arabic version of distress thermometer for Egyptian patients with solid cancers and hematological malignancies

N. Abd El-Azız[1], S. Mohamed[1], E. Kamel[1], G. Elgohary[2]
[1]Assiut University; [2]Ain Shams University

Objective: The distress thermometer (DT) has been studied and validated as an effective screening tool for identifying distress among cancer patients worldwide. To the best of our knowledge, this is the first study to evaluate the validity of the Arabic version of the DT in Egyptian patients with different solid and hematological malignancies. We aimed to determine if this Arabic version is feasible, to define the optimal cutoff value of that version for detecting clinically significant distress, and to determine whether there is any correlation between clinically significant distress and other demographic and Problem List variables.

Methodology: The original form of the DT was translated to Arabic using a forward and backward translation method. Then, 2 groups (solid tumors and hematological malignancies) of Egyptian cancer patients who received chemotherapy and followed up regularly at three different Tertiary-care centers (Ain Shams University Hospital, South Egypt Cancer Institute, and Assiut University Hospital), were enrolled. Those patients had completed a socio-demographic and clinical status questionnaire, the DT and the Problem List scale, and the Hospital Anxiety and Depression Scale (HADS).

Results: The study included a total of 322 patients, 188 (58%) of them were males. They included 182 (56%) patients with solid tumors (82 (45%), 67 (37%), and 33 (18%) with lung, breast and colon cancer, respectively), and 140 (44%) patients with hematological malignancies (lymphomas 68 (48%), acute leukemias 15 (11%), chronic leukemias 47 (34%), and multiple myeloma 10 (7%), respectively). Receiver operating characteristic (ROC) curve analyses showed an area under the curve of 0.72 when compared with a HADS cutoff score of 15. The DT had the best sensitivity (0.74) and specificity (0.65) with cutoff score of 4. Among patients with solid tumors, a DT score of 4 or more was found to have a statistically significant correlation with male gender, advanced cancer stages and most of the Problem List items, including depression, fears, nervousness, sadness, loss of interest in usual activity, religious concerns, appearance, fatigue, indigestion, memory and concentration, nausea, and sexual problems. On the other hand, among those with hematological malignancies, a DT score of 4 or more was found to have a significant correlation with female gender, advanced cancer stages and most of the Problem List items, including child care, work or school, treatment decision, dealing with children and partners, depression, fears, nervousness, sadness, religious concerns, appearance, bathing/dressing, breathing, diarrhea, fatigue, feeling swollen, fever, getting around, indigestion, memory and concentration, nausea, and pain. Interestingly, a multivariate regression analysis confirmed only advanced cancer

Conclusion: The Arabic version of the DT was found to be a valid tool for screening distress in Egyptian patients with solid tumors and hematological malignancies. This study proposes using a cutoff score of 4 as an indicator of clinically significant distress among those populations. Regardless the type and location of malignancy, cancer patients share common distressing symptoms that needs be managed.

OP-24

The current situation of multiple myeloma in Azerbaijan

C. Asadov, A. Shirinova, A. Hasanova, Z. Alimirzoyeva
Institute of Hematology and Transfusiology

Objective: Multiple myeloma (MM) is a clonal plasma-cell neoplasm that activate impulse hematopoiesis, osteoclastic bone resorption, and monoclonal paraprotein in serum and/or urine. The median age at the time of diagnosis varies from 60 to 70 years. The incidence of MM varies widely in different regions of the world. While MM remains an incurable pathology, and therefore the main goal of treatment is to prolong the overall survival. This indicator varies from country to country and depends on the quality of the medical care provided. The aim of this study was to estimate the prevalence, incidence and characteristics of patients with multiple myeloma in Azerbaijan.

Methodology: 272 patients with newly diagnosed MM between 2011 and 2017 were included. An analysis was made of the distribution of MM patients by sex, age, life expectancy after diagnosis, clinical and laboratory characteristics of patients, blood group distribution (blood donors as control group) and seasonality were studied, and the evaluation of treatment was conducted. The prevalence of MM was defined as the total number of live patients at the end of the year to the average annual population, recalculated by 100 thousand people. Statistical analyzes performed by SPSS using chi square test.

Results: The age-adjusted incidence is 1.38/100,000 for males and 1.24/100,000 for females. Average age at diagnosis is 59±10 (30-95): male 59±9.8 and female 59±9.8. The distribution of patients in the economic-geographical zones is such: the highest incidence is in the most urbanized Absheron, and the lowest in Nakhichevan. Average life expectancy is 39.2±26.7 months: male 38.7±26.6 and female 39.3±26.7 months. Laboratory results (average): Hb level - 79±25 g/L, albumin level - 39±10 g/L, Ca level - 2.43±0.72 mmol/L, creatinine level – 158±133 µmol/L, sedimentation - 63.2±20 mm/h, bone marrow plasma cells - 30.3±14%, blood protein level - 96.8±26 g/L. Majority of our patients were treated with VAD 34%, MP 21% and VCD 21% regimens. 31% of patients were diagnosed in stage I or IIA, 69% in stage IIB or III. Primary presentation of disease - 42% bone lesion, 14% dyspneas, 4% tumor formation, 4% infection, 36% others. Complications - 41% fractures, 37% acute kidney failure, 17% neuropathy, 5% transformation into acute leukemia. Blood group association between patients and control group: there is a high risk in A (p=0.0035) and B (p=0.0033), low risk in 0 (p=0.0001) patients. Between group AB results was not statistically significant. Also, there is low risk between Rh positive, high risk between negative patients. (p<0.0001). Seasonality results was not statistically significant. Overall survival improved after borthezomib therapy. Overall survival >90 month was in 35% of patients.

Conclusion: Recent advances in the treatment of MM, have resulted in an improved survival rate. The results of epidemiological studies have shown that the prevalence of MM in our country is one of the lowest in Europe. Though treatment so far do not correspond to those obtained in developed countries.

OP-25

CYP3A5*3, CYP3A4*18 and CYP2B6 gene polymorphisms in chronic myeloid leukemia patients in Azerbaijan

C. Asadov[1], N. Karimova[2], A. Hasanova[1], A. Shirinova[1]
[1]*Institute of Hematology and Transfusiology;* [2]*Institute of Genetic Resources*

Objective: Chronic myeloid leukemia (CML) is a clonal myeloproliferative increase of altered, primitive hematopoietic progenitor cells marked by reciprocal translocation t(9; 22)(q34; q11) and BCR-ABL gene fusion. CML management was dramatically changed by imatinib mesylate (IM), a selective tyrosine kinase inhibitor, which is specifically designed to block the expansion of cells expressing not only BCR-ABL but also receptor of stem cell factor, c-kit tyrosine kinases, and platelet-derived growth factor. However, despite being a gold standard drug for CML treatment, some patients fail to reach the expected results and develop resistance to the drug. Those cases can be explained by various factors such as mutations of BCR-ABL domain or genetic variability of enzymes involved in drug metabolism, including family of cytochrome P450 (CYP). As it is known, IM is metabolized mainly by family of cytochrome P450 (CYP). Polymorphisms of CYP genes can alter the enzyme activity of IM and may affect its response. The aim of the study was to analyze CYP3A5*3, CYP3A4*18 and CYP2B6 gene polymorphisms in CML patients in Azerbaijan.
Methodology: The 153 CML patients (102 IM resistant and 51 IM good responders) were involved in the study. 100 healthy individuals were examined as the control group. Genotyping of CYP3A5*3, CYP3A4*18, and CYP2B6 was conducted using polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP) technique. The frequencies of polymorphic genotypes among IM-resistant and good-response CML patients, and the genotype association with the occurrence of CML were compared by using the chi-square test.
Results: Study of the distribution of CYP3A5*3 polymorphism in CML patients and controls showed that the frequency of G/G genotype was significantly elevated in the CML patients (99.35%) compared to control (95.0%) with corresponding increase in CYP3A5*3 allele frequency indicating that the presence of CYP3A5*3 allele might represent increased risk of developing CML (χ^2=8.318, p=0.0156). No statistically significant difference was observed between CYP3A4*18 and CYP2B6 polymorphisms in CML patients and controls (respectively χ^2=1.96, p=0.3753 and χ^2=2.48, p=0.2892). Also, no statistically significant difference was found in the distribution of CYP3A5*3 and CYP2B6 polymorphism and their alleles in IM resistant and IM good-response CML patients. For CYP3A4*18 polymorphism, the homozygous wild type (TT) genotype and T allele were statistically significantly higher in IM resistant patients (100%) compared with IM good-response patients (respectively 100% vs. 94.1%, χ^2=6.0055, p=0.0143 and 100% versus 97.05, χ^2=6.054, p=0.0139). No homozygous variant (CC) genotype was detected among both IM-resistant and good responders. No statistically significant difference was found in the distribution of the CYP2B6 polymorphism and its alleles in IM resistant patients compared to IM good-response patients.
Conclusion: Our study suggests that CYP3A5*3 gene polymorphism in CML patients might be associated with increased risk of CML development. Polymorphism of CYP3A4*18 is significantly associated with response to IM therapy. Therefore, pretreatment genotyping of this polymorphism may be important in predicting IM response in CML patients.

OP-26

Rituximab reduction for pediatric advanced-stage Burkitt lymphoma

T. Valiev, A. Popa, G. Mentkevich
Pediatric Oncology and Hematology Research Institute of N. N. Blokhin National Cancer Research Center of the Ministry of Health of Russian Federation

Objective: Rituximab in combination with chemotherapy (B-NHL-BFM 1995, 2004; FAB/LMB96) improved significantly treatment results of pediatric advanced-stage Burkitt Lymphoma (BL). But late-effects and secondary immunodeficiencies (results of rituximab mechanism of action) are serious complications for patients.
Methodology: We included 41 pts (age 3–16 years old) with newly diagnosed advanced-stage (III–IV) BL from January 2009 to June 2019. M:F ratio was 6:1. All pts received treatment by B-NHL-BFM 95 protocol: 5 courses for R3 and R4 risk groups. Rituximab combined with only first 2 courses of chemotherapy (AA+R and BB+R) and after disease response assessment pts continued treatment by standard B-NHL-BFM 95 protocol (CC-AA-BB).
Results: Treatment protocol B-NHL-BFM 95 + rituximab was high effective. Event-free survival (EFS) was 90.2±0.5% (median follow-up 92.2+/–5.0 months), relapse-free survival (RFS) – 97.1±0.2% (median follow-up 101.7±4.1 months), overall survival (OS) – 97.1±0.2% (median follow up 109.9±3.8 months). We registered events: 2 (4.8%) cases of disease progression, 1 (2.4%) early relapse, 1 (2.4%) secondary acute myeloid leukemia (successfully cured with FLAG+Ida treatment regimen and allo-SCT, follow up 4 years). Unfortunately, all cases of disease progression and early relapse were fatal, inspite of second-line therapy (R-ICE regimen). Infusion reactions (IR), associated with rituximab were registered in 32 (78%) pts, as usual during first infusion. IR during and after second rituximab infusion was observed only in 1 (2.4%) case. All IR were classified as grade 2–3. No one case of death associated with rituximab infusion was observed.
Conclusion: Two rituximab infusions are enough for effective induction in treatment of advanced-stage BL. High OS rate (97.1±0.2%) with long follow up (9 years) confirm it.

OP-27

Incidence of venous thromboembolism (VTE) in childhood cancers from a tertiary care centre: a unique registry initiative with an open invitation

M. Alsaleh, A. Alkofide, A. Ali, I. Ghemlas, A. Aljefri, M. Ayas, A. Alseraihy, A. Elenazi, A. Alahmari, I. Alfawaz, D. Bushnak, M. Hazeem, A. Ahmad, N. Farhan, A. Alhmouz
King Faisal Specialist Hospital & Research Centre, Riyadh

Objective: Incidence of venous thromboembolism (VTE) in patients with cancers is a complication believed to have a negative prognostic impact, however limited information is available of the same in pediatric patient population. Pediatric Hematology section of King Faisal Specialist Hospital and Research Centre, Riyadh, manages several cases of childhood cancers with VTE.
Methodology: REDCap (Vanderbilt University) web-based data management module was used to develop registry database after approval of the Institutional Review Board (IRB). Retrospective chart review of newly diagnosed patients with malignancies during 2012 to 2018 was conducted to report incidence and outcomes, while prospectively cases will be enrolled after obtaining verbal consent from the patient or families.
Results: A total of 1775 children with cancers [solid tumors: 54% (962); leukemia: 22% (387); neuro-oncology:16% (277); lymphoma: 8% (149)] were reviewed with an overall VTE incidence of 8% (146/1775) observed, 12% (77/962) in leukemia followed by 8% (77/962) in solid-tumors; 7% (12/277) in neuro-oncology and 4% (10/149) in lymphomas, respectively observed over a median follow-up of 3 years. Majority of Children with leukemia developed VTE in Non-Central Nervous System (CNS): 70%, defined by central venous catheter (CVC)-associated upper- or lower-extremity deep venous thrombosis (DVT); while 30% developed in CNS related to asparginase-associated cerebral venous thrombosis, whereas in solid-tumor cases 60% presented with upfront tumor-thrombus and staged accordingly while 40% developed DVT during treatment. Non-CNS VTE observed in 60% of neuro-oncology cases and 100% lymphoma cases. Three-year overall survival (OS) of the cohort was 80.1%, upon comparison of non-VTE to VTE cases an OS of 80.3% and 76.6% was observed, respectively statistically not-significant (p>0.05); however, a longer follow-up is warranted.
Conclusion: A five-year VTE incidence of 8% observed in our cohort is comparable to published thrombosis risk of 1–37% in children. In leukemia, risk factors for VTE remained CVC and asparginase therapy while in the solid-tumors, tumor-thrombus at disease presentation emerged as a factor worth exploring further - to determine its likely effect on treatment outcomes, treatment delays and survival. Data collected through participation on this registry project will enable us to document the use of thromboprophylaxis

and develop guidelines for the prevention and management of thrombosis in pediatric patients with malignancies.

OP-28

Aza maintenance after consolidation increase RFS in MRDve+ low and not in intermediate risk AML patients

L. Girshova, I. Budaeva, D. Zaytsev, T. Chitanava, I. Rogovaia, R. Badaev, K. Bogdanov, T. Nikulina, J. Mirolubova, D. Motorin, J. Alexeeva, A. Zaritskey
Federal Almazov National Medical Research Centre

Objective: Intensive chemotherapy allows to obtain CR rates ranging from 50 to 80% in adult patients with AML, but relapses still occur in 40 –50% of cases. CBF-AML (t(8;21)(q22;q22) or inv(16)(p13q22)/t(16;16)) and NPM1 mutant AML have a favorable prognosis when treated with high dose cytarabine-based regimens. Nevertheless, a substantial proportion of this patients have disease relapses. High risk of relapse can be identified by monitoring MRD using leukemia specific molecular markers. The prevention of hematologic relapse remains the main goal in the care of patients with AML. Post-remission therapies such as alloHCT decrease the risk of relapse. However, the toxicities may outweight the benefits for patients in first remission who have intermediate or low risk disease. Given lack of benefit observed of conventional cytotoxic drugs as maintenance in AML, agents with alternative mechanisms of action are appealing for investigation. We aimed to determine the efficacy of AZA maintenace for relapse prevention in MRDve+ in low-risk and MRDve- intermediate-risk AML patients post-CT.
Methodology: 24 AML low risk patients with NPM1mut and CBF-AML (median age 44) with detectable RT-PCR MRD after completed consolidation and 19 intermediate risk patients (median age 47) with undetectable MRD were included in this prospective study. «7+3» was used for remission induction and HiDAC for consolidation. Patients received a median of 3 cycles induction/consolidation (range 1-4) prior to HMA. RT-PCR specific for NPM1mut (A, B, and D), RUNX1-RUNX1T1, CBFβ/MYH11 and WT1 in bone marrow samples was performed. All patients had a detectable RT-PCR MRD after consolidation. 20 patients started treatment with AZA (75mg/m^2/day s.c. on days 1–7 every 28 days). A median of 5 cycles were given (range 2–12 cycles) which were usually well tolerated. 23 patients without HMA maintenance therapy were monitored MRD only.
Results: After consolidation in low risk MRDve+ group, median RT-PCR of 0.01% in both groups (range 0.001 2.94% and 0.001 3.8%) was received. After a median follow-up time of 10 mo (range 2–103 mo) from initiation of AZA treatment only 2/12 pts developed a relapse after 8.5 and 17.5 mo. Whereas, 8/12 pts without HMA therapy had relapse. RFS was shorter in patients without HMA maintenance therapy (8.7 mo vs median was not reached, p=0.006). A cut-off level of reduction after induction predicting relapse was 3.7lg for NPM1mut and 2.4lg for CBF-AML (median RFS not reached vs 7.9 mo, p=0.003 CI 95% 4.7–25.1). 7/7 pts with MRD above cut-off levels after induction therapy had relapse in the consequent 12 months without HMA maintenance therapy while 3/3 patients on AZA treatment were in remission (Fisher's exact test p=0.016). Patients with MRD below cut-off levels after induction did not have any differences in early relapses frequencies on AZA therapy (p=1.0). AZA maintenance in intermediate risk MRDve- patients did not improve RFS (p=0.84).
Conclusion: The patients with CBF- and NPM1mut MRDve+ AML have the benefit of AZA maintenance after high dose cytarabine-based consolidation. It was of especial benefit in patients with high level of MRD after induction in this cohort of patients. In contrast, AZA maintenance had no effect on RFS in intermediate risk MRDve– patients.

OP-29

Synchronous gastric malt lymphoma and adenocarcinoma with concurrent pulmonary malt lymphoma

E. Turan Erkek, E. Tukel
The Health Science University, Dr. L. Kırdar Education and Research Hospital

Background: Marginal zone lymphomas (MZLs) are classified by The World Health Organization into 3 subtypes as extranodal marginal zone lymphoma (ENMZL, MALT lymphoma), nodal and splenic MZL. MALT lymphoma arises in a number of epithelial tissues such as the stomach, salivary gland, lung, small intestine, thyroid, skin. In general, chronic immune stimulation is thought to be effective in the pathogenesis due to bacterial, viral or autoimmune stimuli. The prototype is the association of Helicobacter pylori infection with chronic gastritis and the development of gastric EMZL.
Aim: The aim of our case report is to emphasize the importance of the co-use of imaging methods and histopathological evaluation during staging and to remind to keep the possibility of concomitance of multiple malignancies in mind.
Case report: A 64-year-old female patient was admitted to the outpatient clinic with the complaint of diarrhea 10–15 times a day with a gradually increasing frequency for six months. She also had concomitant weight loss and night sweating. The laboratory studies of the patient revealed no abnormal value except for hemoglobin of 11 g/dl, MCV of 75.9, iron of 29 µg/dl, iron binding capacity of 359 µg/dl, ferritin of 44.90, and LDH of 259 U/L. The patient with iron deficiency anemia and gastrointestinal complaints underwent gastroscopy and colonoscopy. The gastroscopy showed a lesion with malignant appearance at the distal of the gastric antrum and the biopsy taken was found to be consistent with adenocarcinoma. PET-CT was taken for preoperative evaluation and staging. Suspicious reactive nodules showing slightly increased F18-FDG uptake in bilateral lung parenchyma were reported. Wedge resection was performed for the lesion developed at the diaphragmatic level of the patient's left lung. The biopsy material was evaluated as CD20-positive mature small B lymphoid neoplasm and MZL was identified. Gastrectomy was performed and CD20, CD3-positive staining along with polyclonal staining showing B cell predominance were detected on the proliferated lymphoid nodule with mucosal-submucosal location at a distance of 7 cm to the tumor which was consistent with maltoma. The patient was postoperatively admitted to our hematology clinic. After bone marrow biopsy was performed which was showed no involvement of lymphoma, the patient started to receive R-CVP therapy. For adenocarcinoma only follow up was recommended.
Discussion: Gastric adenocarcinomas are usually at an advanced stage at the time of diagnosis and only a few of them are of local disease and benefit from surgical intervention. In the preoperative staging, many imaging methods such as computed tomography and PET scan are used.
In cases where imaging methods are insufficient, as in our patient, histopathological evaluation should be carried out by taking biopsies from areas of suspicion. If the lesions visualized in the lung were evaluated as metastasis, our patient could be evaluated as inoperable due to misstaging; however, the second concomitant malignancy was noted thanks to biopsy. With the identification of the lesion in the lung as ENMZL, the gastric adenocarcinoma was classified as early stage, giving surgical treatment chance to the patient.

OP-30

T-cell Brazil project: preliminary results after 2 years of T-cell lymphoma registry

C. De Souza[1], M.T. Delamaın[1], E. Mıranda[1], N. Zıng[2], G.N. Rıbeıro[3], A. Cunha Junıor[4], T. Carneıro[5], A. Van-Den-Berg[5], S. Brasil[6], N. Castro[7], J. Souto-Filho[8], R. Lyrio[9], R. Gaiolla[10], A. Hallack-Neto[11], C. Chiattone[12]
[1]University of Campinas – UNICAMP; [2]Prevent Senior Hospital – SP; [3]Federal University of Minas Gerais – UFMG; [4]UOPECCAN-União Oeste Paranaense de Estudos e Combate ao Cancer; [5]Ophir Loyola Hospital, Belem, PA; [6]FCM da Santa Casa of Sao Paulo; [7]Cancer Hospital of Barretos, SP; [8]Medicine School of Campos, Campos dos Goytacases; [9]State University of Rio de Janeiro – UERJ; [10]Medicine School of Botucatu, UNESP; [11]Federal University of Juiz de Fora, UFJF, [12]Samaritano Hospital of Sao Paulo

Objective: T-cell lymphomas (TCL) are rare and heterogeneous biologically. The available treatments are still limited, despite of new therapeutic modalities. The 2018 Brazilian census informed that the country has approximately 209 million inhabitants, concentrated in the south and southeast, and at the same period, the National Cancer Institute (INCA) estimated 10,180 new cases of all NHL, since a little more than 1200 (11.7%) new cases of TCL. Due to its vast

territory, each region of Brazil has inherent peculiarities, both geographically, as climate, topography, and even demographic, as cultural, schooling, longevity and income per capita. Recognizing this immense disparity, and knowing that these data may affect the epidemiology of the disease, reflecting even in the diagnosis, treatment and results, it was developed a Brazilian registry of TCL.

Methodology: T-cell Brazil Project was designed as an ambispective data collect with diagnosis done from January 2015 until March 2020 using the REDCap electronic data capture tools hosted at Hematology and Hemotherapy Center in the University of Campinas. Tissue biopsies, immunophenotypic markers, and clinical information from consecutive patients at each site will be review by panels of expert hematopathologists every year and classified according to the WHO classification.

Results: On July 2019, a total of 30 centers got approval in their Institutional Review Board (IRB) and others 16 are waiting for decision. Eighteen centers, 14 from Southeast, 2 South, 1 North and 1 Center-West, registered 133 cases and 128 were eligible to analysis (4 had incomplete data and one was not TCL). Their median age was 56 years (19–93); 55% male; and histological types were: 54 peripheral TCL-NOS; 21 Anaplastic large-cell lymphoma ALK-; 15 Angioimmunoblastic TCL; 15 Adult TCL/leukemia; 12 Nasal-NK/TCL, nasal type; 7 Anaplastic large-cell lymphoma ALK+; two Hepatosplenic; one Subcutaneous, Panniculitis type and one associated to Enteropathy; 65% III-IV stage; 52% had B symptoms; 67% lymph nodes involvement; 48% extranodal involvement and 3% had CNS. Eleven cases had progression, 9 after the 1st line treatment. There were 36 deaths, 23 (65%) by lymphoma; 13 (35%) infection (one case was complete remission). With a median of follow-up of 10 months (0.1–43) the 24 month-overall survival by histological types was 100% anaplastic large-cell lymphoma ALK+; 65% Nasal NK/TCL, nasal type; 61% anaplastic large-cell lymphoma ALK-; 42% peripheral TCL-NOS and 24% Angioimmunoblastic TCL.

Conclusion: T-cell Brazil project has many challenges to overcome, but the main one is related to regulatory issues in the different regions of Brazil. As a parallel result to the Registry, the exchange of experience and knowledge, plus the educational network that has been formed, will certainly result in a more accurate diagnosis and better prognosis of these lymphomas in Brazil.

OP-31

SH2-containing tyrosine phosphatase-1 (SHP-1) MRNA expression and its promoter methylation in imatinib response in Egyptian chronic myeloid leukemia patients

N. Elkoney, İ. Diab, M. Dessouky, N. Hamed, W. Delgawy
Faculty of Medicine, Alexandria University

Objective: To study the role of SH2-containing tyrosine phosphatase-1 (SHP-1); mRNA expression and its promoter methylation in imatinib response in Egyptian CML patients.

Background: Treatment of chronic myeloid leukemia (CML) patients with imatinib methylate (IM) has achieved a great success in preventing progression of the disease into more aggressive phases (accelerated and blast phases) making IM a corner stone therapy in treatment of CML patients. Unfortunately, resistance against IM has been developed. Resistance may be BCR-ABL dependent that is related to changes in BCR-ABL fusion gene or protein itself or BCR-ABL independent that is unrelated to BCR-ABL fusion gene or protein. One of the independent mechanisms might be the alteration in SH2-containing tyrosine phosphatase-1 (SHP-1) gene expression. SHP-1 is a protein tyrosine phosphatase that antagonize the kinase activity of BCR-ABL. SHP-1 is expressed in different cells of the body especially the hematopoietic cells. phosphatase Epigenetic methylation of SHP-1 promoter gene might lead to silencing of the gene.

Methodology: 50 people divided into resistant, responder and control groups were included in the study. Determination of expression level of SHP-1 was done using mRNA quantitative reverse transcriptase polymerase chain reaction using taqman assay. Determination of promoter methylation of SHP-1 was done by methylation-specific polymerase chain reaction. Descriptive, analytical and ROC curve analysis were used in this study.

Results: We found that SHP-1 mRNA expression level was significantly higher in the responder group than the resistant group and significantly higher in the control group than the resistant group ($p<0.001$), but no significant difference was found between responder group and control group. In addition, there was a significant difference between resistant group and responder group regarding methylation state of SHP-1 gene. Also, there was significant inverse correlation between SHP-1 mRNA expression level and its methylation state. Furthermore, SHP-1 mRNA level was more sensitive biomarker in predicting imatinib response than SHP-1 methylation state. When combined together, SHP-1 mRNA and its methylation state showed lesser sensitivity & specificity than SHP-1 mRNA expression level. Therefore, SHP-1 mRNA expression level can be used as biomarker for predicting response to imatinib among CML patients.

Conclusion: High expression level of SHP-1 and decreased methylation state of SHP-1 gene might derive a greater benefit from imatinib-based chemotherapy. Whereas SHP-1 low expression level, being an important category of CML cancer, might not show much improvement on imatinib-based chemotherapy and could have a worse prognosis than its SHP-1 high expression level counterpart. In addition, SHP-1 expression level is more sensitive and more specific than its methylation state as predictor for response to imatinib. So, SHP-1 mRNA expression level could be a promising biomarker for prediction of response to IM in CML patients. Methylation of SHP-1 promoter gene interprets the decrease in SHP-1 mRNA level in the resistant cases.

OP-32

A retrospective analysis of peripheral T-cell lymphoma patients: single-center 'real-life' experience

M. Ozbalak, S. Kalayoglu Besisik, M. Guzel Mastanzade, O. Ozluk, A. Ozmen, I. Yonal Hindilerden, M. Yenerel, M. Nalcaci
Istanbul University Istanbul Medical Faculty, Division of Hematology, Istanbul, Turkey

Objective: Peripheral T-cell lymhomas (PTCL) are a heterogeous group, with poor long-term outcomes excluding ALK+ anaplastic large cell lymphoma (ALCL).

Methodology: Herein we represent our retrospective analysis of 61 consecutive PTCL cases diagnosed since 2002. Median observation time was 15 months (1–156 months) Seventeen patients were diagnosed with PTCL NOS, whereas 13, 8, 12, 4, 4, and 3 patients were diagnosed with AITCL, ALK+ALCL, ALK-ALCL, Hepatosplenic TCL, Enteropathy associated TCL and NK/T cell lymphoma, respectively. The median age was 54 (range 21–82) and majority of patients were male (n=45; 74%). Seventy-six percent of patients presented with advanced stage, 65% with B symptoms, and 33% with bone-marrow involvement. IPI score was high-intermediate in 51% and high in 15% of patients. Most common first line treatment was CHOP combination chemotherapy. One patient had first line ABVD as the diagnosis was Hodgkin lymphoma, however, being unresponsive, the revised pathology evaluation and T-cell clonal rearrangement was consistent with PTCL-NOS. Three patients (1 PTCL-NOS, 1 enteropathy associated TCL and 1 NK/T cell lymphoma patients) died due to progressive disease without having chance to be treated.

Results: The median PFS&OS were not reached for ALK+ALCL whereas they were 1(95% CI 0.33–0.60) and 18(95% CI 0.36–0.64) months for the rest of the cohort, respectively. Eighteen patients had auto-SCT and 4 patients had allo-SCT. Among these 4 patients (1 AITCL, 1 PTCL-NOS, 1 hepatosplenic TCL, 1 ALK-ALCL), 2 had previous auto-SCT. Three of them died due to progressive disease (n=1) and infectious complications (n=2). One patient with ALK-ALCL relapsed at the fifth year of auto-SCT, had CR again with CHOEP but relapsed again and underwent allo-SCT after salvage BV&GDP treatment. He is still alive with stable disease at the 109th month of follow-up. Five-year PFS were 66% (95% CI 0.16–0.91) and 9.4% (95% CI 0.01–0.29) for ALK+ALCL and non-ALK+ groups, respectively. Similarly, 5-year OS was 73% (95% CI 0.28–0.93) for ALK+ALCL group and 17% (95% CI 0.07–0.32) for the resting cohort. Progression was associated t-lymphoma type other than ALK+ALCL($p=0.017$), high stage disease ($p=0.002$), platelets <150.000/

mm³ (p=0.035), serum albumin <3.4 g/dl (p=0.032), serum total protein ≤6.2 g/dl (p=0.007), hemoglobin <10 g/dl (p=0.009) and liver involvement (p=0.050) at the time of diagnosis. Although not statistically significant, bulky disease >10 cm (p=0.108), high serum LDH (p=0.076) and bone marrow involvement (p=0.066) were also associated with poor PFS. The multivariate analysis could not be performed technically due to missing data and low number of patients. In the univariate analysis, t-lymphoma type other than ALK+ALCL(p=0.038), serum ferritin level over 400 mg/L (p=0.031), serum albumin <3.4 g/dl (p=0.000), serum total protein ≤6.2 g/dl (p=0.001) and bone marrow involvement (p=0.034) at the time of diagnosis were associated with poor survival rates. Although not statistically significant, bulky disease >10 cm (p=0.097) and hemoglobin <10 g/dl (p=0.078) were also associated with poor outcomes. In the multivariate analysis, only t-lymphoma type other than ALK+ALCL was associated with decreased survival rates. Thirty-nine patients (64%) died in the follow-up. Most common reasons were progressive disease and infections. Four patients developed secondary malignancies (1 esophagus squamous cell cancer, 1 MDS, 1 Hodgkin lymphoma and 1 MM).
Conclusion: Given the biological heterogeneity of T-cell lymphomas and the poor outcomes, new prognostic models and treatment strategies compatible with frailty of heavily treated T-cell lymphoma patients should be evaluated.

OP-33

Characteristics and outcome of patients with hematological malignancy admitted to intensive care unit: a single-centre experience

S. Maqsood, F. Badar, A. Hameed
Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan

Objective: Patients with hematological malignancies admitted to intensive care unit (ICU) have a high mortality rate. The aim of our study is to assess the characteristics and outcome of such patients and to identify factors predicting ICU mortality.
Methodology: This is a retrospective chart review, conducted in the intensive care unit (ICU) of Shaukat Khanum Memorial Cancer Hospital and Research Centre over a period of 5 years, from January 2010 to January 2015.
Results: Characteristics Out of a total of 213 patients there were 150 (70.4%) males and 63 (29.6%) females with the median age of 36 years (18–88 years). Main diagnosis was Non- Hodgkin Lymphoma in 127 (59.6%) patients followed by Hodgkin's Disease 27 (12.7%) and 16 Acute Myeloid Leukemia (7.5%). Most of the patients 154 (72.3%) were on active chemotherapy. Most common reason for ICU admission was a combination of respiratory failure with septic shock (29.6%) followed by septic shock alone (19.7%) and acute respiratory failure (13.1%). Majority of admissions to ICU occurred between day one and five of admission to floor (46.5%, n=99) whereas 49 (23%) patients were taken directly to the ICU. Mainstay of treatment in 38.5% of patients included both invasive ventilation and vasopressor support along with other supportive care like fluids and antibiotics. 23.5% received only supportive management. Outcome Analysis of outcome showed that 119 (55.9%) patients expired while in ICU, 14 (6.6%) patients expired during the same admission on floor after being transferred out of ICU. So ICU survival was 44.1% whereas hospital survival was 37.5%. After the discharge from hospital in stable condition 18 (8.5%) patients were lost to follow up. 62 (29%) patients were alive at thirty days. A total of 33 (15.4%) of patients had survived for one year after ICU admission. 21 (9.8%) of patients are still alive and healthy at a minimum median follow up of one and a half years. Predictors of Mortality: Overall, mechanical ventilation was required in 61% of patients. Out of the patients who expired, 92.4% required intubation, whereas from the patients who survived the ICU stay only 21.3% had needed it. Three or more organ involvement was seen in 12.8% of improved patients and 70.6% of patients who died during ICU stay. Neutropenia did not appear to be a major discriminatory factor, with 33% of improved and 42.9% of expired patients being neutropenic at the time of admission to ICU (p>0.05) Majority of patients from both, the improved and expired group required intubation and vasopressors from day one onwards.
Conclusion: Admission to the intensive care unit in a patient with hematological malignancy is associated with poor outcome and high mortality. Identifying the patients who can benefit from aggressive care and prolonged ICU support is important especially when it comes to countries like ours where there are limited resources and financial restraints. Multi organ damage and requirement of invasive ventilation are two main predictors of increased mortality. Neutropenia is also associated with adverse outcome; however, the difference is not as significant as the other two factors mentioned.

OP-34

Clinical features and possible prognostic factors in patients with marginal zone lymphoma: retrospective analysis from two centers

P. Cömert[1], A. Yıldız[1], M. Albayrak[1], M. Yıldırım[2], M. Tığlıoğlu[1], B. Sağlam[1], S. Maral[1], H. Afacan Öztürk[1], M. Aylı[2], O. Şahin[1]
[1]*Diskapi Yildirim Beyazit Training and Research Hospital, Department of Hematology, Ankara, Turkey;* [2]*Gulhane Training and Research Hospital, Department of Hematology, Ankara, Turkey*

Objective: Marginal zone lymphoma (MZL) is characterized by the proliferation of B cells in mucosa-associated lymphoid tissue, lymph nodes, and the spleen. MZL accounts 5–17% of all non-Hodgkin lymphomas and has an indolent clinical course. MZL includes three subtypes; extranodal, splenic and nodal. The parameters that predict prognosis and the need for treatment are still unclear. The aim of the current study was to examine the impact of parameters on the course of disease and the need for treatment in MZL.
Methodology: A retrospective study was conducted with MZL patients in the Hematology Departments of two centres between 2010 and 2018. The demographic and disease characteristics, and also hematological and biochemical parameters at the time of diagnosis were examined. Using these data, treatment requirements and survival rates were calculated. The effect of the parameters on overall survival (OS) and need for treatment were analyzed.
Results: 40 MZL patients were included in this study. The mean age of patients was 64.13±10.39 and 25 (62.5%) were female. During the follow-up, 25 patients required treatment and 15 patiens were followed up without treatment. OS of all MZL patients was 58.4 months. OS was significantly higher in patients with nodal MZL than in extranodal and splenic MZL patients. OS of patients who required treatment was 92.9 months while untreated patients was 58.4 months and there was no significant difference among the groups. The platelet count of untreated patients at the time of diagnosis were significantly higher than patients who received treatment (p=0.04). No significant relationship was found between any parameter and OS.
Conclusion: We demonstrated platelet count at the time of diagnosis as a predictive factor for future treatment need. It is an objective and simple blood test that may be helpful to predict the course of the disease although further studies are warranted.

OP-35

Outcome of allogeneic stem cell transplant in adolescent and young patients with monosomy 7 in hematological malignancies

S. Ahmed, T. Hussain, S. Hashmi, O. Ahmed, N. Chaudhri
King Faisal Specialist Hospital and research Center

Introduction: Since a report of some 50 years ago describing refractory anemia associated with group C monosomy, monosomy 7 and interstitial deletions of chromosome 7 (del(7q)) have been established as one of the most frequent chromosomal aberrations found in essentially all types of myeloid tumors regardless of patient age and disease etiology. Monosomy 7 or deletion 7q (-7/7q-) is the most frequent high-risk cytogenetic feature reported in acute myeloid leukemia (AML) and is associated with a dismal outcome after chemotherapy alone. Allogeneic stem cell transplantation (SCT) appears to be the best consolidation strategy in these patients (pts), thereby significantly improving outcomes.
Objective: To see the impact of monosomy 7 in the outcome after allo-SCT.
Methodology: We evaluated a retrospective single-center study 67 patients (44 M 23 F) comprised of 61 isolated monosomy 7 and 6 combined with monosomy 7 from 08/1998 to 12/2018. All patients have age group between 14–40 years. The diagnosis included in this study is MDS/AML (52 pts, CML

BLAST CRISIS (2 pts), Fanconi anemia (2 pts), CMML to AML (1 pt), ALL (7 pts), CML with myeloid Blast crisis (3 pts). Most of the transplant carried out in CR 1.

Results: OS is 36% in median follow up of 8 years. DFS is 22%. Cumulative incidence of acute GVHD is 30.7% and death without aGVHD is 11%. Cumulative incidence of cGVHD is 40.4% and death without cGVHD is 32.9%.

Conclusion: SCT in hematological malignancies pts with -7/additional karyotype provides durable response in one third of the pts. Disease status at the time of transplantation remains the strongest prognostic factor for poor outcomes. Relapse and additional karyotyping was the main factor for mortality. In these pts, future efforts should focus on prevention of relapse by therapeutic modalities like early withdrawal of immunosuppression, administration of hypomethylating agents, donor lymphocytes infusion or others.

OP-36

Clinical characteristics of relapsed ovarian cancer patients with striking response to the bevacizumab at first relapse

F. Kose, S. Alemdaroglu, H. Mertsoylu, A. Besen, O. Guler, S. Simsek, G. Erbay, C. Onal, H. Celik
Baskent University

Objective: Ovarian cancer is fifth leading cause of the cancer related death in women. Platin based doublet regimen plus bevacizumab is standard treatment in relapse. The primary aim of this study is to define clinicopathological characteristics of the relapsed ovarian cancer who derived unexpectedly long benefit from bevacizumab treatment.

Methodology: Total number of 106 patients with relapsed ovarian cancer and treated with bevacizumab (bevacizumab is not reimbursed as a part of adjuvant treatment in Turkey) on their first relapse were included. For the purpose of the study, the patients were placed into two groups, Group A and B, selected on the basis of the rate of PFS 1(time between adjuvant chemotherapy start date and first radiological progression) to PFS 2(time between second line treatment and second radiological progression). The patients included into Group A if PFS 1 greater than PFS 2 and Group B vice versa.

Results: Group A and B were consisted of 67 (63%) and 39(37%) patients. At a median follow-up of 32.1 months (5.3–110.8), 56 (52.8%) patients were died. Significant number of patients (78.4%) treated with primary surgery without neoadjuvant treatment and 59(57.8%) out of the 102 patients had debulking surgery when their cancer relapsed. PFS 1 and 2 were estimated as 16.5 months (14.1–18.9) vs 13.7 months (9.9–17.5) and 13.4 months (8.0–18.6) vs 29.7 months (21.5–38.0) in group A and B, respectively ($p<0.001$ and $p<0.001$). Only parameter that show significant difference between groups was the rate of platin resistant patients; Group A: 13 (19.4%) out of 67 patients vs Group B: 15 (38.6%) out of 39 patients with a p value of 0.041. Binary logistic regression indicates PFS1 is significant inverse predictor (shorter PFS-1 means greater chance of being in group B) of entering Group B [Chi-Square=16.5, df=6 and $p=0.011$ (<0.05)]. PFS1 is significant at the 5% level [PFS1 wald=4.33, $p=0.038$ ($p<0.05$)]. In multivariate analysis, cox-regression proportional hazard, cytoreductive surgery at second relapse (yes or no) ($p=0.028$; HR=0.3, 95% CI 0.02–0.7) showed significant effect on PFS-2. On the other hand, platin resistance (<6 months; yes or no) ($p=0.04$; HR=4.0, 95% CI 1.1–14.4) and secondary surgery outcome (no visible vs visible) ($p=0.003$; HR=0.2, 95% CI 0.07–0.58) showed significant effect on OS. Bevacizumab related adverse effects with greater than grad 3 detected in 13 (15%) and 10 (25%) in group A and B ($p=0.77$).

Conclusion: Our findings indicate that bevacizumab can produce strikingly high PFS (over 24 months) in some relapsed ovarian cancer patients whom significant portion of them were platin resistant relapse with short PFS-1. This gain specifically achieved in patients who had aggressive secondary surgery with no-visible surgical outcome.

OP-37

Colon cancer in diabetic patients: does risk affect diagnosis at an early stage?

M. Karaca[1], M. Celik[2]
[1]*Health Sciences University Medical Faculty, Antalya Training and Research Hospital, Medical Oncology, Antalya, Turkey;* [2]*Antalya Kepez State Hospital, Department of Endocrinology and Metabolism, Antalya, Turkey*

Objective: Diabetes mellitus is associated with an elevated risk of colon cancer. A meta-analysis of 14 studies (6 case-control and 8 cohort) estimated that the risk of colon cancer among diabetics was approximately 38 percent higher than nondiabetics. In this study, to determine the effect of diabetes mellitus on diagnosis in patients with colon cancer.

Methodology: The clinical findings of 205 patients with stage I, stage II, stage III, and stage IV colon cancer treated between 2010 and 2016 were retrospectively evaluated. Twenty patients had diabetes mellitus. We analyzed differences in colon cancer metastasis, recurrence, and treatment-related toxicity between patients with and without diabetes. All statistical analyzes were performed using the "Social Sciences Statistical Package" version 22.0 for Windows (SPSS, Armonk, NY: IBM Corp.). P values less than or equal to 0.05 were considered significant. For descriptive analysis, categorical variables were defined as frequency. Distribution with percentage and quantitative variables was given as median, minimum and maximum values. Chi-square or Fisher's exact test was used for categorical variables.

Results: The number of patients with diabetes mellitus was 20 (9.8%) and 185 (90.2%) without diabetes. The mean age of the patients with diabetes was 65.1±10.7 years and the mean age of the patients without diabetes was 61.2±11.5 years. female/male ratio was 11/9 in diabetic patients and female/male ratio was 69/11 in non-diabetic patients. 4 (20%) of the diabetic patients were stage 1, 10 (50%) were stage 2, 5 (25%) were stage 3, 1 (5%) was stage 4. 27 (14.6%) of the non-diabetic patients were stage 1, 122 (65.9%) were stage2, 21 (80.8%) were stage3, 15 (8.1%) were stage4. There was no statistical difference between the two groups in terms of stage ($p=0.268$). No recurrence was seen in diabetic patients, whereas recurrence was found in 13 (7%) of non-diabetic patients ($p=0.015$). While distant metastasis was not detected in diabetic patients, distant metastasis was observed in 10 (5.4%) of non-diabetic patients ($p=0.014$). There was no statistically significant difference between the two groups in terms of chemotherapy response ($p=0.844$). In terms of side effects of treatment, no toxicity was seen in diabetic patients after the first stage treatment, whereas 7 (3.8%) of non-diabetic patients had toxicity. however, there was no statistically significant difference between the two groups in terms of toxicity ($p=0.376$).

Conclusion: We think that diabetic patients who are examined at 3-month intervals are important factors in the diagnosis of colon cancer in the early stage

OP-38

Initial presentation of prostate cancer may hint different clinical characteristics along with serving predictive biomarker in castration-resistant prostate cancer patients treated with abiraterone acetate

F. Kose[1], A. Sedef[2], A. Besen[1], H. Mertsoylu[1]
[1]*Baskent University Adana Hospital;* [2]*Tarsus Medical Park Hospital*

Objective: Advanced prostate cancer (PC) can be diagnosed either de-novo metastatic disease (DNM) or relapse (Later metastatic-LM). There is urgent need for the predictive biomarkers to define patients who derived most benefit from next-generation AR axis inhibitors. The aim of this study is to investigate predictive role of initial presentation on CRPC patients treated with abiraterone acetate.

Methodology: The clinical data of 111 CRPC patients treated with abiraterone acetate between 2012 and 2017 was retrospectively analyzed. The patient and tumor characteristics of DNM and LM were detailed.

Results: At a median follow-up of 51.8 months (4.7–211.2), 60 (54.1%) patients were died. The DNM and LM groups were consisted of 66 (59%) and 44 patients (41%), respectively. OS and PFS were estimated as 21 months (95% CI 18.5–23.7) and 9.5 months (95% CI 6.6–12.4) for whole group. PFS of the

LM and DNM were found as 11.1 (95% CI 6.0–16.1) and 8.4 (95% CI 6.0-10.7) months, respectively (p=0.35). OS of the LM and DNM were found as 22.0 (95% CI 18.0-26.1) and 19.1 (95% CI 14.5–23.8,) months, respectively (p=0.35). In univariate analysis, presence of oligometastases (p=0.04), rate of primary resistance (p=0.001) and PSA response (50% or 90%) (p=0.001 and p=0.001) showed significant effect on PFS.

Conclusion: Our findings indicate that abiraterone is effective treatment option for the both LM and DNM PC patients. Although, LM PC patients had significantly shorter castration sensitive period, abiraterone provide significantly higher PSA response rate, show similar primary resistance rate and produce numerically higher survival time compared to DNM group.

OP-39

The predictive value of MRI and ^{18}F-FDG-PET/CT for assessing pathological response in locally advanced rectal cancer after neoadjuvant chemoradiotherapy

G. Guler Avcı[1], I. Aral[2]
[1]Gaziosmanpasa University, Faculty of Medicine; [2]Nevşehir Public Hospital

Objective: Recently, organ protection approaches come to the forefront in local advanced rectal cancer (LARC). Surgery was omitted in patients who responded well to neoadjuvant therapy with a "wait and see" policy in some studies. In order to do this, the complete clinical response (cCR) must be determined with very good reliability. For this purpose, we evaluated the role of MRI and ^{18}F-FDG PET CT in determining the correct stage and predicting the pathological response. The correlation between clinical staging and pathological staging was examined.

Methodology: Seventy six patients with pathologic proven rectal adenocarcinoma, clinical stage IIA–IVA, received neoadjuvant chemoradiotherapy (CRT) were evaluated retrospectively from August 2014 to March 2019 in Gaziosmanpaşa University Faculty of Medicine Radiation Oncology Clinic. External radiotherapy was administered with intensity modulated radiotherapy (IMRT) with simultaneous integrated boost (SIB) technique as a total dose of 45–50 Gy in 25 fractions with 1.8–2 Gy doses per day and concomitant oral capacitabine at a dose of 825 mg/m^2 was given in the majority of patients (85%). Pelvic MRI, colonoscopy and ^{18}F-FDG PET CT were performed for evaluated the clinical stage before the neoadjuvant treatment (NAT) decision. After NAT, re-evaluation MRI and PET CT were done after an average of 6–8 weeks after completion of RT.

Results: Median follow-up time was 25 months (range, 3–57 months). Fifty-eight patients (78.4%) underwent surgery but 16 patients (21.6%) refused surgery. Three patients had complete pathological response (pCR) to NAT. Down staging was recorded in 80% (n=46) of 58 patients who underwent surgery. Sphincter preservation was achieved in 13 of 25 patients with tumors located in the lower rectum, only 12 patients underwent APR. There were no statistically significant differences between both MRI and PET CT with pathology results in terms of response evaluation. As a result of the comparison of MRI and PET CT with pathological results; sensitivity and specificity were 88.4% (38/43) and 36.4% (4/11) for MRI and 100% (41/41) and 98% for PET CT, respectively. The positive predictive values (PPV) were similar for PET CT and MRI (84.4% vs 85.4%), while the negative predictive value (NPV) was 44% for MRI and 100% for PET CT.

Conclusion: Both PET CT and MRI are effective in evaluation of response to NAT and are predictive of pathological response.

OP-40

Colchicine and serum CA72-4 elevation

M. Gürbüz[1], D. Tutar[2], P. Kubilay Tolunay[3], B. Karaalioğlu[3], E. Yekedüz[3], M. Karaoğlan[4], G. Utkan[1]
[1]Ankara University Faculty of Medicine, Department of Medical Oncology; [2]Ankara University Faculty of Medicine, Department of Cardiology; [3]Ankara University Faculty of Medicine Department of Medical Oncology; [4]Ankara University Faculty of Medicine Department of İnternal Medicine

Objective: Tumor markers are biochemical indicators of the presence of neoplastic proliferation.CA-72-4 antigen, first discovered in the early 1980s, is an antigenic marker of glycoprotein TAG-72, which is also recognized by the B72.3 and CC-49 monoclonal antibodies. Colchicine is a drug that binds to the intracellular tubuline protein and shows antimitotic activity by inhibiting new microtubule polymerization. Colchicine disrupts neutrophil chemotaxis by reducing the expression of adhesion molecules in membranes such as L-selectins and E-selectins. Here we report serum CA 72-4 elevation in a patient receiving colchicine for pericardial effusion.

Case report: The laboratory tests of a 62-year-old female patient who was admitted to an external center with the complaints of chest pain, malaise, palpitation revealed leukocytosis and elevated sedimentation and CRP. The thoracic computed tomography (CT) of the patient who was found to have cardiomegaly on posterior anterior chest radiography was reported as 'There are pericardial fluid measuring 2 cm at the most prominent level and a significant contrast uptake on pericardial leaflets. Multiple lymphadenopathies (LAP), the largest of which measuring 24×10 mm at perivascular space, are present in mediastinum perivascular space, subaortic, subcarinal and paratracheal areas. No pleural fluid was visualized.' The patient was admitted to our clinic with the pre-diagnosis of perimyocarditis, tuberculosis, malignancy, and rheumatic disease.The transthoracic echo-cardiography of the patient showed 0.9 cm behind the left ventricle during diastole and minimal pericardial fluid around other cardiac cavities. Pericardial fluid increase was observed. The findings may be suggestive of pericarditis". The patient who was consulted with cardiology department was initiated on ibuprofen and colchicine. The quantiferon and sputum tests ordered with the pre-diagnosis of tuberculosis were negative for acid-resistant bacilli (ARB) and the tuberculin test was measured as 2 mm and the tuberculosis culture showed no growth. ANA, RF, anti-CCP, anti-DS DNA, ANCA, anti-SSA, anti-SSB, anti-Jo1, anti-Ro-52, AMA, anti CMV IgM, anti-CMV IgG, EBV-VCA IgM, EBV-VCA IgG and Brucella agglutination test were negative. The blood, urine and sputum cultures ordered showed no growth. The tumor markers of CA-72-4: 300 U/mL; CEA, CA-19-9, CA-15-3, AFP were normal. Endoscopy, colonoscopy and breast ultrasonography (USG) of the patient with elevated CA-72-4 revealed no pathological finding. The positron emission tomography (PET) CT of the patients revaled increased ^{18}F-FDG uptake on mediastinal lymph nodes (SUV max: 6.8) and pericardium (SUV max: 4.9). The patient who was found to have pathological contrast uptake on lymph nodes on PET CT underwent endobronchial ultrasonography (EBUS), and fine-needle aspiration biopsy was taken from subcarinal 7 and 11L lymph node stations. The cytopathological diagnosis came back negative for malignancy. CA-72-4 elevation was considered to be associated with colchicine, so colchicine was discontinued. Follow-up CA-72-4 level of the patient ordered about 3 weeks later came back normal.

Conclusion: It is important to check the patient's medications when unexpected tumor marker concentration increases are documented. Studies investigating the relationship between drugs or supplements and tumor marker increases are needed.

OP-41

The efficacy of postoperative radiotherapy in fibromatosis

H.S. Arslantaş[1], E.B. Yılmaz[2]
[1]Çukurova Üniversitesi; [2]Mersin Üniversitesi

Objective: Fibromatosis is a benign mesenchymal neoplasm originating in the superfisial or deep muscular structures. The efficacy of radiotherapy was evaluated retrospectively in our series of 11 patients with fibromatosis who underwent postoperative radiotherapy. Since the size of the tumor is large and the tumor is infiltrative, the possibility of total excision is low. The aim of this study was to show the efficacy of radiotherapy in decreasing the number of repeated surgery and loss of tissue in this tumor group

Methodology: Postoperative radiotherapy was given to 11 patients diagnosed with fibromatosis in the Department of Radiation Oncology, Faculty of Medicine, Çukurova University between 2012–2019. Of all, 4 (36%) have aggressive fibromatosis and 7 (64%) have superficial fibromatosis. The ratio of male to female is 4 to7, their ages were 25–64 years and the median age was 45. The aggressive fibromatosis were located in lower extremities in 2 patients, in paravertebral region in 2 patients and pelvis in 1 patient.

The superficial fibromatosis locations were as following; lateral thoracic wall in 1 patient, supraclavicular region in 1 patient, lower extremities in 2 patients, axillary region in 2 patients, forearm in 1 patient. Size of the tumors was between 8 cm and 25 cm (median 14 cm). Four of the patients with superficial fibromatosis underwent surgery two times before radiotherapy. Radiotherapy was delivered with normal fractionation and single doses of 1.8 to 2 Gy with 6–18 MV photon or electron energy with linear accelerator as conformal radiotherapy. Postoperative radiotherapy doses for microscopic and macroscopic residual diseases were 50–54 Gy and 56–60 Gy, respectively. Response assessment and post-treatment follow-up for radiotherapy were performed according to the RECSIT criteria by computed tomography (CT) or magnetic resonance imaging (MRI).

Results: Median follow-up period was 46 months (range 3–84 months). Of 7 patients with superficial fibromatosis, 5 (71%) had microscopic residual tumor (R1) and 2 (29%) had macroscopic residual tumor (R2) postoperatively. In cases with aggressive fibromatosis; 1 (25%) had microscopic residual tumor and 3 (75%) had macroscopic residual tumor. Patients were evaluated with CT or MRI findings at the first follow-up at 3 months after radiotherapy according to RECIST criteria. Early and late side effects have been reported according to RTOG criteria. Complete respond (CR) was seen in 2 patients with superficial fibromatosis with R2 tumor,stabil disease (S) in 2 patients and parsiyel response (PR) in 1 patient with aggressive fibromatosis with R2 tumor were detected. None of the patients had grade III-IV early side effects. In the late period, grade II neurotoxicity was detected in 2 cases and grade III joint toxicity was observed in one case due to fibrosis.. In cases with superficial fibromatosis, 3 and 5-year local control rates (n=2) were 100%. Local control rates of 3 and 5 years could not be evaluated in patients with aggressive fibromatosis due to short follow-up periods. One patient with R2 tumor and aggressive fibromatosis had progression (P) at 13th month. This patient was treated with Tamoxifen 20 mg and observed as stable in the routine controls at 12 months after progression.

Conclusion: The low number of the patients in the study limited the statistical evaluation of the results but however the efficacy of postoperative radiotherapy was seen in the patients with superficial fibromatosis with R1-R2 group. Moreover in many studies radiotherapy was stated as an effective treatment in patients with aggressive fibromatosis to prevent the increase of infiltrative potential of the tumor and to increase the local control rate with recurrent surgeries.

OP-42

Efficacy of therapeutic plasma exchange in the treatment of multiple myeloma patients with hyperviscosity syndrome: a single-centre experience

Z. Cvetkovıc[1], A. Kulic[2], R. Markovic[3], A. Strugar[2]
[1]Medical Faculty University of Belgrade, Belgrade, Serbia, Department of Haematology Clinical Hospital Centre Zemun, Belgrade, Serbia; [2]Department of Transfusiology Clinical Hospital Centre Zemun, Belgrade, Serbia; [3]Department of Nephrology Clinical Hospital Centre Zemun, Belgrade

Objective: Multiple myeloma (MM) is a group of mature B cell neoplasms characterized by clonal proliferation of plasma cells and a subsequent secretion of paraprotein (M protein) – monoclonal immunoglobulins (Ig) or their fragments such as light chains (kappa and lambda). Overabundance of monoclonal Ig increases blood viscosity and may lead to hyperviscosity syndrome (HVS). HVS is seen in 2–6% MM patients at presentation, more often in IgA MM. This severe clinical condition is the main cause of early mortality in MM patients and represents the treatment of choice for therapeutic plasma exchange (TPE), according to ASFA (American Society for Apheresis) guidelines. As plasmapheresis removes just the circulating paraproteins, the decrease in serum viscosity and the improvement of symptoms are short-term, so the definitive treatment of HVS is treatment of the underlying MM. Objective of the study is to evaluate the efficacy TPE in MM patients presented with HVS

Methodology: Total of 65 consecutive MM patients – 32 males and 33 females mean age at diagnosis 65 years (range 44–88) diagnosed and treated at the Department of hematology Clinical Hospital Center Zemun during five years period (2013–2018), were included in the study. Of this cohort, 43 pts had IgG MM (27 IgG kappa and 16 IgG lambda), 11 pts had IgA MM (7 IgA kappa and 4 IgA lambda), 10 pts had light-chain MM (6 kappa and 4 lambda), and 1 pt had nonsecretory MM. Advanced disease i.e. Durie-Salmon CS III had 55(83.3%) pts at presentation, and 21(32.2%) pts had chronic renal failure as well. Their median overall survival (OS) was 30 months.

Results: Clinical and laboratory signs of HVS were present in 12/65(18.5%) pts with MM (8 with IgG MM, and 4 with IgA MM; female:male = 7:5) at presentation. Their mean total protein concentration was 121.3 g/L (range 112–138), and mean monoclonal Ig concentrations were as follows: IgG 65.6 g/L and IgA 72 g/L. Neurological symptoms were dominant in 8 pts, bleeding tendency was present in 2 pts and heart failure in 2 pts. Urgent TPE were performed in all 12 pts (2–7 procedures/pts, median 4 procedures/pt), and after the confirmation of MM diagnosis the cytoreductive therapy was initiated. TPE resulted in the disappearance of clinical signs of HVS in 11/12 pts, and after the first course of chemotherapy total protein levels were normalized in 10/12 pts (1pt refused the suggested chemotherapy, and 1pt died of congestive heart failure). No adverse effects were documented during TPE treatment.

Conclusion: According to our experience, TPE proved safe and effective for the treatment of HVS in MM. Higher than expected prevalence of HVS in our group of patients is the consequence of advanced MM stage at diagnosis.

OP-43

The effect of chemotherapy on survival applied in the last term of life in cancer patients

U. Isik[1], A. Erol[1], Y. Cakmak[1], E. Ozden[1], U. Kefeli[1], D. Cabuk[1], K. Uygun[1], M. Simsek[2]
[1]Kocaeli University; [2]Yozgat City Hospital

Objective: Cancer is an increasing health problem worldwide and leads to an important socioeconomically load in the community, material and spiritual losses in individuals. Chemotherapy is the common name of treatment applied by biological, synthetic, and hormonal agents against rapidly proliferating cells like cancer cells. Chemotherapy in the last term of life is a frequently debating subject nowadays and data in the literature is poor. In patients with short life expectancy, administration of chemotherapy is still a controversy because of toxicity and lack of clear clinical benefit. We aimed to evaluate the efficacy of chemotherapy applied in the last term of life in cancer patients, and if there is a difference between overall survival times of patients that received chemotherapy in the last 30 days before death and more than 30 days before death

Methodology: Patients referred to our center between January 2015 and December 2017 was included. We described patients who received chemotherapy in the last 30 days before death as Group 1; patients who received chemotherapy more than 30 days before death as Group 2. Demographical features of the patients, treatment regimens, cause of death, and overall survival time were analyzed.

Results: A total number of 359 patients that received chemotherapy at least once in their lifetime were evaluated. There was statistically significant difference between two groups in overall survival times after diagnosis (165 days for group 1 and 308 days for group 2, p=0.000). There was also statistically significant difference between two groups in terms of median survival times after last chemotherapy administration (12 days for group 1, and 62 days for group 2, p=0.001)).For both groups, there was significant difference between underlying diagnoses in terms of overall survival.

Conclusion: We found a statistically significant difference between two groups in terms of overall survival time and median survival time after last chemotherapy administration. Because a short survival time was observed in patients that received chemotherapy in the last 30 days of their lifetime, chemotherapy for these patients should be considered after detailed assessment. Future studies will provide more data in this patient population.

OP-44

Evaluation of platelet functional assay and investigation of its importance in patients

N. Shagerdi Esmaeli[1], A. Homafar[2], M. Hamidpour[1]
[1]Department of Hematology and Blood Banking, Shahid Beheshti University of Medical Science, Tehran, Iran; [2]Department of Dietitian and Nutrition of Azad Islamic University, Tabriz, Iran

Objective: Platelets have a pivotal role in the initial defense against insult to the vasculature and are also recognized of critical importance in the acute care settings of percutaneous coronary intervention and cardiopulmonary bypass. In these environments both platelet count and function may be markedly compromised. Unfortunately, current assays to evaluate the parameters of platelet count and function are of limited utility for bed-side testing. Moreover, it is suggested that there may be significant inter patient variation in response to antiplatelet therapy that may be exacerbated by other agents (e.g. heparin) that are routinely administered during cardiac intervention.
Methodology: Here we describe a practical, rapid and user-friendly whole blood platelet function assay that has been developed for use in bed-side settings. Platelet agonists were formulated with an anticoagulant and lyophilized in blood collection tubes standardised to receive a l mL fresh whole blood sample. In the presence of an agonist, platelets are activated and interact (aggregate). Using traditional cell counting principles, non-aggregated platelets are counted whereas aggregated platelets are not. The percentage (%) of functional platelets in reference to a baseline tube may then be determined.
Results: Results are available within four minutes. Platelet aggregation in whole blood demonstrated good correlation with turbidometric aggregometry for both ADP (r=0.91) and collagen (r=0.88). Moreover, in clinical settings where antiplatelet agents were administered, this rapid, bed-side, platelet function assay demonstrated utility in monitoring patient response to these therapies.
Conclusion: This novel bed-side assay of platelet function is extremely suitable for the clinical environment with a rapid turn-around time. In addition, it provides a full haematology profile, including platelet count, and should permit enhancement of transfusion and interventional decisions.

OP-45

Quality of life and activity and participation of children with acute lymphoblastic leukemia are associated each other

F. Ipek, V. Yıldız Kabak, M. Dogan, S. Atasavun Uysal, T. Duger
Hacettepe University

Objective: Recent studies reported that children with acute lymphoblastic leukemia (ALL) had an impaired body function and these might be associated with decreased quality of life, activity limitation and participation restriction. For this reason, the aim of this study was to assess quality of life and activity and participation in children with ALL and to investigate relationship between them.
Methodology: This study was conducted at Hacettepe University, Department of Physiotherapy and Rehabilitation, Oncological Rehabilitation Unit in Turkey. Children with ALL between 5 to 10 years of age were included in this study. They received outpatient-based chemotherapy. Quality of life in children was assessed with Pediatric Quality of Life Inventory (PedsQL) 3.0 Cancer Module. This module consists of 8 sub-groups; pain and hurt, nausea, procedural anxiety, treatment anxiety, worry, cognitive problems, perceived physical appearance, and communication. Activity and participation of children was evaluated with Pediatric Outcome Data Collection Instrument (PODCI) parent report. The PODCI subscales comprise the following fields: Upper Extremity Function, Transfers and Basic Mobility, Sports and Physical Function, Pain/Comfort, Happiness, and Global. All statistics were calculated with SPSS Version 23. Spearman correlation coefficient was used to examine the association between quality of life and activity and participation. Statistical significance was defined as p value less than 0.05.
Results: Fifteen children with ALL (8 girls, 7 boys) were recruited. Their mean age was 7±1.37 years. Mean PedsQL Cancer Module scores for self-report and parent-report were 75.62±12.06 (min.53.85 - max.90.39) and 75.77±14.21 (range 54.41–94.57), respectively. In addition, mean PODCI score was 87.80±7.87 (72.00–97.00). There was a moderate association between scores of PedsQL cancer module parent-report and PODCI (r=0.560, p=0.30). Furthermore, there were high associations between treatment anxiety and worry subgroup of PedsQL cancer module self-report and happiness subtest of PODCI (r=0.740, p=0.002 and r=0.883, p=0.000, respectively).
Conclusion: This study shows that quality of life and activity and participation in children with ALL are related each other. Because of high anxiety and worry levels of children, they have decreased quality of life and limited activity and participation. Therefore, the addition of emotional and psychosocial components to their treatment may be effective.

OP-46

HBA1C level correlation with iron deficiency anemia

A. Homafar[1], Z. Aaghamohammadpour[2], F. Manzoor[2], P. Yari[3], N. Shagerdi Esmaeli[4]
[1]Department of Nutrition and dietitian, Islamic Azad University, Tabriz, Iran; [2]Department of Laboratory Science of Azad Islamic University, Tabriz, Iran; [3]Department of Laboratory Science of Azad Islamic University, Marand, Iran; [4]Department of Hematology and Blood

Objective: Hemoglobin A1C (HbA1c) reflects patient's glycemic status over the previous 3 months. Previous studies have reported that iron deficiency may elevate A1C concentrations, independent of glycaemia. This study is aimed to analyze the effect of iron deficiency anemia on HbA1c levels in diabetic population having plasma glucose levels in control.
Methodology: Totally, 120 diabetic, iron deficient anemic individuals (70 females and 50 males) having controlled plasma glucose levels with same number of iron-sufficient non-anemic individuals were streamlined for the study. Their data of HbA1c (Sebia capillary piercing), ferritin (Immulite 2000 XP ECLIA hormone analyzer), Fasting Plasma Glucose (FPG, Roche Hitachi P800/917 chemistry analyzer), Hemoglobin (Siemens2120i), Peripheral Blood Smear examination (Wright-Giemsa staining), Red cell indices, and medical history were recorded. Statistical analysis was carried out by student's t-test, Chi-square test, and Pearson's coefficient of regression. Data collected from central Laboratory of Shohada E Tajrish Hospital, Tehran, Iran.
Results: We found elevated HbA1c (6.8±1.4%) in iron-deficient individuals as compared to controls, and elevation was more in women (7.02±1.58%). On further classification on the basis of FPG levels, A1C was elevated more in group having fasting glucose levels between 100–126 mg/dl (7.33±1.55%) compared to the those with normal plasma glucose levels (<100 mg/dl). No significant correlation was found between HbA1c and ferritin and hemoglobin.
Conclusion: This study found a positive correlation between iron deficiency anemia and increased A1C levels, especially in the controlled diabetic women and individuals having FPG between 100-126 mg/dl. Hence, before altering the treatment regimen for diabetic patient, presence of iron deficiency anemia should be considered.

OP-47

Production of immortal squamous cell line from larynx carcinoma

A. Demirci[1], Y. Doğruyol[2], S. Yıldırım[2], L. Uzun[3], S. Aşkın[4], İ. Akalın[5]
[1]Kartal Anatolian Imam Hatip High School; [2]Istanbul Medeniyet Universty, Medical School; [3]Istanbul Medeniyet Universty, Department of Otorhinolaryngology; [4]Kartal Anatolian Imam Hatip High School, Department of Biology; [5]Istanbul Medeniyet Universty, Department of Medical Genetics

Objective: Cancer is characterized by uncontrolled cell proliferation and is one of the most common cause of deaths worldwide including Turkey. Treatment modalities are in improvement and developed from long lasting investigations where the experimental processes with in-vitro cell lines are the must. Hence different types of cell lines are being used in cancer researches. They are largely derived from cancer cells with or without using gene suppression methods of vectors, viruses and recently CRISPR technologies. However, because of cost limitations those cell lines are brought

abroad in Turkey that increases the budget of our researches and declining the researches due to long lasting gathering period. In this study, we aimed to produce our own immortalized squamous cancer cell line to be used in our own scientific studies.

Methodology: In this project we obtained a squamous cell line that has unlimited division ability and can be used in squamous cancer research. Characterization will be continued. After obtaining the approval of the local ethics committee (2018/0502) and consent of the patient, 1 cm^3 laryngeal tumor tissue was taken from the patient and physically disintegrated in the cell culture laboratory, cultured with RPMI Complete Medium (RPMI CM) in proper petri dishes and entitled İMU-KAİHL-Lx 1.0 cell line. RPMI CM was changed every 72 hours and cell division ability was examined on inverted microscopy. Trypsin method was applied for passages and renamed accordingly as IMU-KAİHL-Lx 1.1 and IMU-KAİHL-Lx 1.2. After observing relevant cell division ability, the cells were frozen in cryovial tubes with 2 ml RPMI freezing medium that contains 20% FBS and 10% DMSO and stored (approximately 8×10^6 cells) in liquid nitrogen tank for further investigations while the remaining cells in the petri dish continued to be grown. The squamous cancer cell lines were characterized using PCR and gel electrophoresis based short replication regions (STR) analyses.

Results: Approximately 10×10^6 cells obtained from 1 cm^3 larynx tumor sample. The obtained cells were determined squamous cell type by using inverted microscope. The first tumor cell line of our university was obtained and produced from the larynx squamous carcinoma cells.

Conclusion: Here, we successfully produced a squamous cell line obtained from primary larynx tumor of a patient that could be used for squamous cancer researches. The characteristics of the cell line were similar compared with the other cell lines in the literature according to length measurements of these repeated sequences on the DNA. Thus we believe we could use it for our experiments. Further cell lines from various tumors might be included to study to achieve more prone and diverse immortalized cells.

OP-48

Measurable residual diseases in haematological malignancies: current applications and future direction

S. Bakr[1], G. Elgohary[2]

[1]Faculty of Medicine, Fayoum University, [2]Faculty of Medicine, Ain Shams University

Introduction: Minimal/measurable residual diseases represents an independent prognostic indicator for several haematological malignancies helping to predict clinical outcome and enables for further assessment of the effectiveness of treatment. The methods of detection of MRD has remarkably improved regarding sensitivity and specificity, and different methods such as real time quantitative polymerase chain reaction (RQ-PCR), multi-parametric flow cytometry (MFC), digital PCR or next generation sequencing (NGS) are currently used in clinical practice. However, the best method still needs to be determined.

Methodology: MFC is a crucial clinical tool for detecting MRD particularly after the recently developed protocol of the EuroFlow consortium which attains detection with reproducibly high sensitivity (10–5–10–6). Recently, Digital PCR has been adopted for quantitative assessment of MRD. It is superior to RQ-PCR in term of simplicity, as it does not require calibration curve. Although it is cheaper than NGS, it cannot detect MRD when new mutations occur. NGS represents a useful tool to monitor MRD, however its current major drawback is the lack of international accepted standardization.

Results: While enhancement in standardization of the different MRD approaches was reported, optimal timing and specific threshold for intervention need to be defined.

Conclusion: Therefore, well-designed clinical studies are required to diminish the risk of relapse and improve overall survival.

OP-49

Comparison of quality of life between early and advanced stage ovarian cancer patients

Y. Yalcın[1], M. Karaca[2], S. Erıs Yalcın[3]

[1]Department of Obstetrics and Gynecology, Istinye University School of Medicine; [2]Department of Medical Oncology, Health Science University School of Medicine, Antalya Training and Research Hospital; [3]Department of Obstetrics and Gynecology, Suleyman Demirel University School of Medicine

Objective: Approximately 225,000 new cases of ovarian cancer are diagnosed worldwide each year. The standard approach for treating patients with ovarian cancer is surgery followed by platinum and taxane based chemotherapy (CT). Quality of life (QoL) and well-being are affected by different physical, social, spiritual and mental factors. Immediately after diagnosis of cancer, most patients focus on anticancer treatment and its challenges. In this situation the primary objective of treatment is to cure the disease and secondary to maintain the best possible QoL. Since survival rates and life expectancy after treatment for cancer are rising due to more effective therapies, so more focused on QoL. The aim of this study was to compare of QoL outcomes in women underwent surgery and chemotherapy for early and advanced stage ovarian cancer.

Methodology: A cross-sectional study was performed in 47 successfully treated ovarian cancer patients in Antalya Training and Research Hospital. To assess QoL we used the European Organization for Research and Treatment of Cancer (EORTC) QLQ-OV28 standardized questionnaire. The included patients were informed about the aims of the study and written informed consent was obtained. Patients with epithelial ovarian cancer between 18 and 70 years of age who had received the last chemotherapy at least 6 months ago were included. Exclusion criteria were: concurrent malignancies, inability to understand and complete the questionnaire. All patients were under surveillance after primary treatment without evidence of disease. The EORTC QLQ-OV28 module includes seven multi-item scales (gastrointestinal symptoms, peripheral neuropathy, other chemotherapy side effects, menopause-related symptoms, body image, attitude to disease and treatment, and sexual functioning). We linearly transformed the EORTC QLQ-OV28 data to yield scores from 0 to 100; higher scores are equivalent to worse or more symptoms except for sexual function items where higher scores indicate better QoL. Patients were stratified into two groups and compared as follows: early stage versus advanced stage. Statistical analysis of variance with post hoc test and Fisher's exact test was employed to compare groups. A p value <0.05 was considered statistically significant.

Results: In total, 60 ovarian cancer patients were invited to participate, of which 47 women (78.3%) responded. Twenty-six patients were advanced stage and 21 patients were early stage. The mean age of patients with early and advanced stage group were 56.5±8.7 and 58.3±9.1 years, respectively (p=0.232). There was no statistically significant difference between the two groups with regard to all other patient characteristics; body mass index (32.3±6.6 vs 33.1±5.7, p=0.341), menopausal status (71.4% vs 76.9%, p=0.435) and histological types (80.9% vs 84.6%, p=0.367). There was no significant with respect to differences between the groups for the EORTC QLQ-OV28 scales; gastrointestinal symptoms (32.4±21.3 vs 27.6±14.3, p=0.226), peripheral neuropathy (21.3±22.6 vs 27.3±25.1, p=0.625), other chemotherapy side effects (34.9±15.7 vs 37.3±12.4, p=0.542), menopause-related symptoms (38.2±28.6 vs 39.1±28.3, p=0.763), body image (44.3±21.1 vs 45.2±19.2, p=0.342), attitude to disease and treatment (80.7±24.5 vs 81.2±19.1, p=0.875) and sexual functioning (39.5±14.2 vs 41.1±14.8, p=0.789).

Conclusion: There was no clinically important difference in the quality of life in patients with either early or advanced ovarian cancer. QoL outcomes matter to patients for well-being.

OP-50

Evaluation of secondary hypogammaglobulinemia in patients with hematologic malignancy receiving ibrutinib therapy

S. Çelik, Z. Güven, L. Kaynar, B. Eser, M. Çetin, A. Ünal
Erciyes University, Faculty of Medicine, Department of Hematology

Objective: Hypogammaglobulinemia (HG) is characterized by a decrease in total serum immunoglobulin(Ig) levels and can lead to immunodeficiency associated with recurrent and severe infections and is a common complication of B-cell malignancies, such as chronic lymphocytic leukaemia (CLL), non-Hodgkin lymphoma(NHL), multiple myeloma and Waldenström Makroglobulinemia (WM). HG also increases with the treatment of B cell malignancies. Ibrutinib is one of these treatments and acts by inhibiting bruton tyrosine kinase. In this study, we investigated secondary hypogammaglobulinemia(SHG) in patients with hematologic malignancies receiving ibrutinib therapy.
Methodology: 24 patients were included who were followed in the Hematology Department of Erciyes University, who had been treated with Ibrutinib for at least 3 months. 20 of them have CLL, 3 have Mantle Cell Lymphoma (MHL) and 1 had WM. IgG levels were measured before Ibrutinib and after 1, 2, 3 ,6, 9 and 12 months of Ibrutinib treatment. Intravenous immunoglobulin(IVIG) treatment was initiated in patients with frequent infections and IgG levels below 500 mg/dL. Demographic characteristics of patients receiving and without IVIG treatment were compared, but no statistically significant difference was observed. Previous treatments of the same group of patients were compared and no differences were found. Significant differences were observed in IgG and Hb levels in laboratory values (p=0.005 and 0.008, respectively). IgG values were compared.There was a significant decrease in IgG levels after Ibrutinib treatment (p=0, 001).
Results: SHG may develop both from the B cell malignancies itself and the drugs used in the treatment and this situation predisposes to infections. Infections are the most important cause of mortality and morbidity in these diseases. Recommended measures to prevent infection in SHG include Ig replacement, prophylactic antibiotics and vaccination. Of these, only Ig replacement is shown to reduce major infections in SHG, but this comes at considerable cost. B cell-targeted therapies such as anti-CD20 antibodies, Bruton tyrosine kinase inhibitors, Phosphoinositide 3 kinase δ inhibitors and chimeric antigen receptor T cells may cause SHG. Ibrutinib inhibits bruton tyrosine kinase so blocks B cell receptor signaling, induces apoptosis and prevents malignant B cells from adhering to micro-environment cells. In our study, there was a significant decrease in IgG levels after Ibr treatment(p=0.001).A total of 5 patients received IVIG treatment, but 4 of them received IVIG replacement prior to Ibr treatment, but IgG levels were significantly decreased despite IVIG replacement after Ibr treatment. There was no statistically significant difference between the two groups in terms of age, sex, time of diagnosis, duration and type of treatment, bulky disease and genetic factors. Significant differences were observed in IgG and Hb levels in laboratory values. IgG and Hb were 737 mg/dL, 11.2 g/dL g in patients receiving IVIG and 1,270 mg/dL, 13.5 g/dL in patients not receiving IVIG, respectively (p=0.005, 0.008).
Conclusion: SHG may develop in patients with CLL,NHL and WM especially with B cell based therapies such as Ibrutinib and may cause frequent infections in this group of diseases. In our study, SHG was evaluated after Ibr treatment. IgG levels were significantly reduced; therefore, IgG levels should be closely monitored in patients receiving Ibrutinib and IVIG replacement is very important when necessary.

OP-51

Recognizing genetic susceptibility in children with leukemia and lymphoma: the current state in European centers

Jelena Lazic
Department for hematology and oncology, University Children`s Hospital Belgrade, Medical School University of Belgrade, Serbia

Background: Leukemia and lymphoma (L&L) have traditionally been regarded as sporadic, non-hereditary, diseases. Except for some overt, but very rare familial cases, genetic studies in L&L have focused on acquired somatic mutations to enable precise diagnostics and guide target treatment. However, in the era of NGS technologies, germline mutations predisposing to pediatric L&L have increasingly been described and some recent studies estimate that 16–20% of pediatric leukemias may have a germline predisposing condition. Germline mutations address clinical management of a patient and the family and modify follow up in comparison to sporadic cases. The current clinical practice of recognizing genetic predisposition in pediatric L&L patients is still in its infancy and specific training and support networking are highly recommended.
Method: To identify specific needs for training and support networking regarding recognizing genetic susceptibility in children WG5 of CA16223 launched a survey to map the current clinical practice of recognizing genetic predisposition in pediatric L&L patients. A team of pediatric hematologists/oncologists and geneticists drafted a questionnaire (Q) that was sent to national centers in 25 countries across Europe directly or via the European Reference Network-Paediatric Cancer (ERN PaedCan).
Results: In total, 95 centers from 25 countries (18 HIC and 7 M IC) responded with questionnaires (13 Qs via ERN PaedCan), providing information regarding 8391 patients/year. Several tools are available to guide pediatric hemalologists/oncologist to recognize genetic susceptibility in children (Jongmans, Percept, Ripperger, Brozou, SEHOP-PETHEMA). Remarkably, more than half of the centers (59%) did not use any tools when taking a family history (FH), which was taken for 89% of patients. In 18% of centers there was no regular team discussion (TD) regarding patients with suspected genetic predisposition. The composition of the team in TD was highly variable between centers, even within the same country. The need for specialized training for hematologists and geneticists was indicated by 84%, the need of a European support network was advocated by 78% and the need of transparent legislation and uniform policy considering specific ethical, legal and socioeconomic implications of a diagnosis of hereditary susceptibility to L&L in a child/adolescent patients was indicated by 58% of responders.
Conclusions: To meet the request of specific training 'LEGEND' has organized a training school (TS) that was attended by 36 trainees from 20 countries. Trainees were selected among 74 participants, mostly young paediatric hematologists/oncologists and geneticists. However, it was felt that also senior colleagues in the feild of pediatric oncohematology may benefit from an up-date on the recent insights in the genetic heredity of L&L. A workshop with this aim will be held in October 2019 and multiple training occasions are planned for the next years.

Poster Presentations

Adult Hematology

PP-01

Infected herpes zoster in a chronic lymphocytic leukemia patient treated with ibrutinib

M. Okay, Y. Buyukasik, S. Aksu, I. Haznedaroglu, N. Sayinalp
Hacettepe University, School of Medicine

Objective: Herpes zoster (HZ) is caused by the reactivation of varicella zoster virus (VZV). HZ is presented as a painful vesicular dermatome eruption [1]. Herpes zoster's clinical course may be more severe in immune-compromised patients [1]. In this case report, we aimed to present HZ infection in a patient with CLL on ibrutinib treatment.

Case report: A 72-year-old female patient was followed up in our center with the diagnosis of CLL since 2010. She was previously treated with fludarabine, cyclophosphamide, rituximab (FCR), rituximab, chlorambucil for CLL. Ibrutinib was started eight months ago for relapsed CLL. The patient was admitted to hospital with complaint of pruritis and vesicular eruption in her neck. There were no fever and pain. There were bullous lesions in her neck, right ear, inferior of face. Her hemoglobin level was 11.2 g/dl, leukocyte count was 18.8×10^9/L, absolute neutrophil count was 2×10^9/L and lymphocyte count was 11.4×10^9/L. The patient was hospitalized for HZ. The skin biopsy was performed and resulted positive for herpes zoster. Her immunoglobulin G level was 530 mg/dl. Intravenous immunoglobulin 400 mg/kg/day was started. Acyclovir intravenously 600 mg 3 times a day was started. After three days, ampicillin/sulbactam 1500 mg four times a day, intravenously, was added for the treatment due to superinfection of HZ. After nine days, the lesions did not decrease. The patient had fever (38.3°C) so; ampicillin/sulbactam treatment was switched to tigecycline. Tigecycline was stopped after 7 days. After 14 days, the lesions were regressed and acyclovir was stopped. Valacyclovir orally 1 g/day was started. Tramadol was started because of post-herpetic neuralgia. The patient is still receiving tramadol for her pain. One month after hospitalization, her ibrutinib was re-started without any complication.

Ibrutinib is an oral, irreversible inhibitor of Bruton's tyrosine kinase (BTK). In the literature, opportunistic infections including with HZ were reported in patients who had treated with ibrutinib [2]. Also, there were case reports with respect to visseral VZV infections in ibrutinib and idealisib treatment in relapsed CLL [3].

Generally, HZ infection is benign and limited. However sometimes, it may show a more serious clinical course in immune-compromised patients [1].

Conclusion: The HZ in a patient with hematologic malignancy should be treated more carefully. In this case report, a HZ infection may be relatively resistant to the treatment. The antiviral and antimicrobial prophylaxis is important in CLL patients on ibrutinib treatment. As in this patient, prolonged prophylaxis with valacyclovir should be remembered in patients with herpes zoster.

References

[1] Dayan RR, Peleg R. Herpes zoster — typical and atypical presentations. Postgrad Med 2017;129(6):567–71.
[2] Byrd JC, Brown JR, O'Brien S, et al. Ibrutinib versus ofatumumab in previously treated chronic lymphoid leukemia. N Engl J Med 2014;371:213–23.
[3] Giridhar KV, Shanafelt T, Tosh PK, Parikh SA, Call TG. Disseminated herpes zoster in chronic lymphocytic leukemia (CLL) patients treated with B-cell receptor pathway inhibitors. Leuk Lymphoma 2017;58(8):1973–6.

PP-02

NG2 expressin in adults acute myeloid leukemia in Egypt

A. Gawaly, A. Allam
Tanta University

Background: Acute myeloid leukemia (AML) is a hematopoietic stem cell disorder characterized by a block in differentiation of hematopoiesis, resulting in growth of a clonal population of neoplastic cells or blasts. AML causes are still unknown; however, it can be clinically manifested using Flowcytometry analysis.

Aims: To assess NG2 expression in adult acute myeloid leukemia patients and its correlations to disease free survival.

Methodology: 30 Patients were divided into three groups, 1) 11 males (55%); 2) 9 females (45%); 3) 10 control patients with pancytopenia rather than malignancy they were 5 males (50%) and 5 females (50%). Cases were diagnosed on the basis of clinical presentation, morphological and cytochemical smears of peripheral blood and BMA as well as immunophenotyping criteria for diagnosis of AML.

Results: Patients different groups showed no significance in sex or age. Hepatosplenomegaly was observed in 45% of patients, fever 45%, lymphadenopathy 15% and bleeding 25%. Complete blood count showed significant decrease of hemoglobin level in AML patients, while total leucocyte count, LDH, ESR showed increases in patient compared to control group. Expression of NG2 in AML patients was 40% negative and 60% positive expression, while control group was negative expression. CBC, blast percentage in P.B and B.M and survival rates showed differences in NG2+ve group and NG2-ve percentage.

Conclusion: Analysis of NG2 expression has a major role to be used as a prognostic marker. NG2 could be a target for therapy by using anti NG2 antibody in a subset of AML patients who does not respond to conventional therapy.

PP-03

The significant application of the 4T criteria in assessing the proper need for a HIT study assay in a Saudi tertiary care hospital

G. Elgohary[1], F. Qahtani[1], T. Elhassan[1], F.T. Shah[2]
[1]*King Saud University, College of Medicine;* [2]*Ain Shams University*

Objective: Heparin-induced thrombocytopenia (HIT) is a life-threatening complication of exposure to heparin that occurs in a small percentage of patients exposed, regardless of the dose, schedule, or route of administration [1]. Heparin induced thrombocytopenia (HIT) results from an autoantibody directed against endogenous platelet factor 4 (PF4) in complex with heparin. This antibody activates platelets and can cause catastrophic arterial and venous thrombosis with a mortality rate as high as 20 per cent [2]. Diagnosis of HIT relies on clinical suspicion determined by 4T score and testing for anti-PF4/heparin antibodies. Clinical practice guidelines published by both the American College of Chest Physicians and British Society for Standards in Hematology recommended the use of the 4T score before ordering the immunoassays as a measure of pretest probability[2,3]. The purpose of this study is to evaluate the utilization of 4T score before ordering anti-PF4/heparin antibodies in the Hospital and to assess the impact of the 4T score would have had on the utilization of the HIT antigen test [3].

Methodology: It was a retrospective chart review for patients who are 18 years or older, admitted in King Khalid University Hospital between January 1, 2016 and February 28, 2016, and had a HIT assay performed. After calculating 4T score retrospectively, we calculated the proportion of patients who had 4T score documented prior to Immunoassay testing and proportion of this tests, which were not indicated due to low 4T score

Results: Of a total of 111 patients in 205 tests were ordered by physician only 99 tests were performed due to non-convenience of the indication of the test. Out of the 111 patients, 27 of the patients received low molecular weight heparin (enoxaparin) and the remaining received unfractionated heparin. None of the patients received LMWH had a positive HIT assay. Out of the 29 patients received standard unfractionated heparin, 8 subjects had a positive HIT assay, 1 with a low probability 4T score, 4 with an intermediate probability 4T score and 3 with high probability 4T scores. 2 patients developed thrombosis and one of them with intermediate probability and the other one with high probability.

Conclusion: The HIT assay is still over utilized in our clinical setting even after the validation of 4T score criteria in the system 8/111(7.2%) tests were positive. Half of the patients admitted in the Intensive care units and the remaining in the general ward. Hopefully the mandating of 4T criteria in the

system decrease the unnecessary HIT assay by 50% which were rejected by the lab system. Still we are questioning the insisting of the clinical physicians in ordering the HIT assay even without calculating the 4T criteria

PP-04

Outcome of autologous stem cell transplantation in multiple myeloma, in the era of novel agents: a single-centre experience

V. Bafna[1], S. Damodar[2], C. Bendi[2]
[1]Oncolife Cancer Centre; [2]Narayana Hospital

Objective: Multiple myeloma (MM) is characterized by the neoplastic proliferation of a single clone of plasma cells producing a monoclonal immunoglobulin. In the last decade the major advance in the management of MM has been the introduction of novel agents Thalidomide, Bortezomib and Lenalidomide into the therapeutic armamentarium. The novel agents along with ASCT have markedly improved the rate of complete remission, which has important implications in overall outcomes.
Methodology: We retrospectively analysed the data in patients with multiple myeloma who were transplanted at our centre from 2015 to 2018. Aim was to analyse the influence of pre transplant characteristics and post-transplant treatment modalities on progression free and overall survival.
Results: A total of 50 MM patients with median age of 55 yrs (38 to 67 years) were transplanted between 2015 and 2018. Male to female ratio was 1.27:1 with 28 (56%) male and 22 (44%) females. In all, 38 (76%) patients had IgG, 7 (14%) had IgA and 2 (4%) had light chain. Twelve (24%) patients were classified as ISS I whereas 25 (50%) were ISS II and 13 (26%) were ISS III. At the time of ASCT, 34 (68%) of patients were in complete remission (CR), 14 (28%) in very good partial remission (VGPR) and 2 (4%) patients were in partial remission (PR). Prior to autograft, 76% (38) of cases had received VTD regimen whereas 24% (28) had received VCD regimen. Conditioning with melphalan 200 mg/m^2 was given in 44 (88%) of patients, remaining 6 (12%) patients received 140 mg/m^2 in view of renal failure. Following ASCT 48 (96%) patients achieved CR/VGPR at 3 months excluding 2 (4%) patients who had TRM. All patients were advised at 3 months post-transplant for maintenance therapy with thalidomide/lenalidomide. Over a median follow up period of 46 months, 28 (56%) of the patients were alive and disease free, 11 (22%) were alive with relapse, and 9 (18%) had disease related mortality. Median OS and PFS from the date of transplantation were 40 and 26 months respectively. Median OS from diagnosis was 46 months.
Conclusion: Autologous stem cell transplantation in combination with novel drugs is an effective strategy in patients with MM to improve depth of response, PFS, and overall survival.

PP-05

Determination of the best cut-off metaphase percentage for discrimination of aging- versus myelodysplasia-related loss of Y chromosome

E. Aladag, A. Dogan, A. Karatas, H. Goker, Y. Buyukasik
Hacettepe University

Objective: Loss of Y chromosome (LOY) is a possible chromosomal event occurring in bone marrow of the healthy elderly. On the other hand, this phenomenon may also be associated with hematopoietic neoplasms as a clonal aberration. It is one of the relatively frequent cytogenetic abnormalities in myelodysplastic syndrome (MDS) that is also used for prognostic classification of this neoplastic disorder. The diagnosis of MDS, which is mainly a disease of elderly, frequently depends on confirmation of clonality by cytogenetic analysis of the bone marrow. Whether there could or not be a sensitive and specific level of LOY discriminating clonal loss versus age-related loss has not been properly investigated. We aimed to determine the most optimal cut-off level differentiating between MDS-related clonal versus age-related normal LOY if present.
Methodology: Bone marrow cytogenetic analysis database of our hospital was screened to find LOY cases that were finally diagnosed with MDS depending on revised WHO 2016 diagnostic criteria and those without any hematopoietic neoplasms. The optimal cut-off level of LOY for discrimination of these two groups was determined with receiver operating characteristic analysis.
Results: There were 76 cases with LOY. 27 of them were diagnosed with MDS and 17 were assigned to the control group. An 80% cut-off value had the best discriminating capacity. This level provided an acceptable specificity (89%) at the expense of a low sensitivity (36%).
Conclusion: It was impossible to describe an ideal cut-off level for LOY differentiating between MDS and normal controls. A LOY level higher-than 80% can be confidently accepted as compatible with MDS, but the majority of MDS cases had lower values.

PP-06

Unclassifiable non-CML classical myeloproliferative diseases with microcytosis: findings indicating diagnosis of polycythemia vera masked by iron deficiency

E. Aladag, S. Aksu, H. Demiroglu, H. Goker, N. Sayinalp, İ. Haznedaroglu, O. Ozcebe, Y. Buyukasik
Hacettepe University Department Hematology

Objective: Polycythemia vera (PV) is a myeloproliferative disorder characterized by overproduction of morphologically normal red blood cells (RBCs), granulocytes, and platelets, a phenotype that is caused by a mutation (V617F) in Janus kinase 2 (JAK2). However, JAK2 V617F is also found in approximately 50% of patients with essential thrombocytosis and primary myelofibrosis, rendering its presence nonspecific as a diagnostic test. An increased red cell mass is a major criterion for the diagnosis of PV according WHO 2016 criteria. High hemoglobin (Hgb) or Hematocrit (Hct) are universally used as indicators of an increased red cell mass for the diagnosis of PV. However, conditions such as iron deficiency (ID) with decreased mean cell volume may mask the diagnosis due to non-elevated Hct level. The aim of this study was to investigate the clinical characteristics of the patients with unclassifiable non-CML classical myeloproliferative disease with microcytosis (MPD/M) and non-elevated Hgb and Hct levels at diagnosis and to determine if some of these cases could be real PV cases masked due to ID-related microcytosis.
Methodology: There were 23 MPD/M cases among 208 non-CML classical MPD cases (11%). Among 22 patients who had adequate test results related to the cause of microcytosis, ID and beta-thalassemia trait were the apparent causes of microcytosis in 15 and 1 cases, respectively.
Results: Clinicopathological correlations revealed consistently positive JAK2 V617F mutation status (20/20, 100%), frequently elevated RBC count (17/23, 73.9%), and PV-compatible bone marrow findings (10/12, 83.3%). These findings are compatible with PV instead of essential thrombocytopenia or primary myelofibrosis. In spite of frequent cytoreductive use 3 cases developed increased Hgb/Htc levels during median 58.2 (279-63) months' follow-up.
Conclusion: These data show that the majority of MPD/M cases are PV patients masked due to ID related microcytosis.

PP-07

Single-center experience: comparison of reduced intensive chemotherapy and low-dose cytarabine treatment as remission induction in older age aml cases

A. Senturk Yikilmaz, S. Akinci, S. Bakanay, İ. Dilek
Yıldırım Beyazıt Üniversity, Division of Hematology, Ankara

Objective: The aim of this study was comparison of treatment with reduced dose of cytosine arabinose (100 mg/m^2, continuous intravenous infusion) and daunorubicin (45 mg/m^2 2–3 days) treatment protocol versus low dose cytarabine (2×20 mg/m^2 10 days/28 days) treatment as the remission induction treatment of aged 65 years and older AML patients.
Methodology: The data of the over the age of 65 years of cases diagnosed as AML between 2010 and 2018 at Hematology Clinic of Atatürk Training and Research Hospital were retrospectively analyzed. Statistical analyzes were performed using chi-square test using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). A value of less than 0.05 was considered significant.

Results: Clinical and laboratory findings at the time of diagnosis were compared according to the treatment choice. Mean survival of 59 patients was 19±3.9 months. The mean survival of the patients who received Ara-C + daunorubicin treatment and low-dose cytarabine treatment was 26.4±6.2 and 14.8±4.1 months, respectively (p=0.044). After the first induction treatment, 16 (27.1%) cases were obtained in all series recovery in peripheral blood, and 12 (75%) of these patients were treated with Ara-C + daunorubicin (p=0.001). Total survival of 21 (35.6%)cases with neutrophil recovery at the first month and 38 (64.4%) cases without neutrophil recovery at the first month were 36.1±7.7 and 5.8±0.9 months, respectively (p=0.001) The OS was 27.7±5.4 months in patients with platelet recovery at the first months of induction treatment, while the OS 2.1±0.2 months in the patients who had no platelet recovery at the first months of induction treatment (p=0.001). The OS of the patients with erythrocyte recovery at the first months of induction treatment was 29.6±5.7 months, while the OS of the patients without erythrocyte recovery was 2.4±0.3 months (p=0.001). Among 41 (69.5%) patients treated with low-dose ARA-C, the number of patients with ANC ≥0.5×10^3 cells/μL at the end of the first month was 7 (17.1%). The mean duration of neutrophil recovery was 21 days. The survival rates of cases with neutrophil recovery events and those without neutrophil recovery were 25.9±14.6 months and 5.8±0.9 months, respectively (p=0.001).

Conclusion: The choice of treatment for advanced age AML patients is decided by considering the performance status and comorbid diseases of the patient. Although the duration of hospitalization was longer in patients with reduced intensive chemotherapy, we found that this group had higher neutrophil recovery and longer total survival. We found that the absolute neutrophil count at ≥0.5×10^3 cells/μL (recovery of neutrophil) at the first months of induction treatment as low-dose ARA-C in patients with advanced age AML was associated with an increase in overall survival.

PP-08

A descriptive study of multiple myeloma in Algerian population

O. Ibtissem, M. Hacene, G. Sabiha, G. Farida
Faculty of Medicine, Badji Mokhtar University, Annaba, Algeria

Inroduction: Multiple myeloma is a neoplastic disorder characterized by proliferation of a single clone of plasma cells derived from B cells. This clone of plasma cells proliferates in the bone marrow and frequently invades the adjacent bone, producing skeletal destruction that results in bone pain and fractures. The diagnosis depends on identification of abnormal monoclonal plasma cells in the bone marrow, M-protein in the serum or urine, osteolytic lesions, and a clinical picture consistent with multiple myeloma

Objective: To determine the clinical and laboratory features of patients with diagnosed multiple myeloma.

Methodology: Records of all patients in whom multiple myeloma was initially diagnosed at department of hematology, from January 1, 2010, to December 31, 2016, were reviewed.

Results: Of the 172 study patients, 18% were younger than 50 years, and 25% were 70 years or older. The median age was 61 years. Of these 172 patients, 50% were men. Anemia was present in 34% of patients, bone pain was present at diagnosis in 75% of patients. Serum protein electrophoresis revealed a localized band in 82% of patients, immuno-fixation showed a majority of the myeloma proteins (50%) were of the IgG isotype followed by IgA(23%), whereas light-chain myeloma was present (18%), IgM (9%). A monoclonal light chain was found in the urine in 54%. The age and sex distributions of our patients were similar to those of patients with multiple myeloma seen in Tunisia and Morocco. Clinical history was taken in all our patients and the major presenting complaints were recorded. Bone pain was one of the chief complaints in 75% of our patients. In studies by Gupta and Kyle, 79% and 58% patients respectively had bone pains at diagnosis. Generalized weakness and fatigability were recorded in 34% of our patients and in 32% patients in a study of the Mayo clinic. Similarly, raised serum creatinine levels were found in 50% of the patients, for who these results were available, compared with only 55% and 48% patients in two studies by Kyle and al.

Conclusion: Multiple myeloma accounts for about 1% of all types of malignancy and slightly more than 10% of hematologic malignancies. The reported increased incidence during the past few decades is probably related more to the increased availability of medical facilities for elderly patients and to improved diagnostic techniques than to an actual increased incidence. A better understanding of the biology of myeloma means that quite soon we might be able to define and tailor-make at diagnosis which patients will most readily respond to which biological treatments.

PP-09

Blastic plasmacytoid dendritic cell neoplasm: a rare case report

Ş. İzmir Güner
Memorial Şişli Hospital

Objective: Plasmacytoid dendritic cells were first identified 50 years ago by Lennert and his associates. BPDCN is a rare, highly aggressive hematopoietic malignancy that is characterized by cutaneous infiltration with or without bone marrow involvement. Its overall incidence is extremely low. The leukemic form of the disease is very rare.

Case report: A 35-year-old female patient presented to our department with a cutaneous lesion especially on her right shoulder also at the whole body. Laboratory data disclosed anemia (hemoglobin 9.3 g/dL) thrombocytopenia (59×10^9/L) and 60% morphologically immature atypical cells in the peripheral blood. Bone marrow aspiration showed 88% infiltration of immature blast cells with the following immunophenotype: CD45(+), CD25(+), CD43(+), CD103(+), CD38(+), CD56(+), CD19(−), CD5(−), CD10(−), CD20(−), CD4(+), NG2(+). Chromosomal alterations were detected by cytogenetic analysis of the bone marrow In the cytogenetic analysis, a pathologic karyotype was found as (46,XX),t (9;11) (p21;q23)/47,si+19/51,sdl1,+6,+8,+9,+21. Also MLL was positive. She had axillary, jugular, submandibular, and supraclavicular lymphadenopathy. Cutaneous, lymph node, and bone marrow biopsy confirmed the diagnosis of blastic plasmacytoid dendritic cell neoplasm (BPDCN). She was treated with cyclophosphamide, vincristine, adriamycin, and dexamethasone (HYPER-CYVAD) as part of an acute lymphoblastic leukemia treatment-protocol. She achieved first complete remission. Due to the highly aggressive type of leukemia, we decided to continue with induction 2 chemotherapy (etoposide-cytosine arabinoside), but she died 5 months after the first sign due to multiorgan failure.

Discussion: Plasmacytoid dendritic cells were first identified 50 years ago by Lennert and his associates. BPDCN is a rare, highly aggressive hematopoietic malignancy that is characterized by cutaneous infiltration with or without bone marrow involvement. Its overall incidence is extremely low. The leukemic form of the disease is very rare. BPDCN predominantly affects males, and generally the elderly. The majority of patients present with asymptomatic solitary or multiple cutaneous reddish-brown nodules. Clinically, this malignancy generally presents in the skin, often followed by bone marrow and blood involvement. However, any organ can be affected. The disease follows a short course and fulminant leukemia is the common terminal stage. Diagnosis is based on the expression of CD4, CD56, and CD123 in the absence of T-cell, B-cell, or myeloid markers. Although identification of the immunophenotypic features of BPDCN has improved its recognition, this entity remains diagnostically challenging. Insufficient knowledge of this entity and inadequate immunophenotypic investigation can lead to the misdiagnosis of a different leukemia. The prognosis of patients with BPDCN is poor, with a median survival of 12 months regardless of treatment type. Acute lymphoblastic leukemia-type treatment regimens are advised and a promising initial response may occur, but this is followed by quick relapse. There is also the option of bone marrow transplantation for young patients with an acceptable performance status.

Conclusion: In conclusion, we encountered a rare type of leukemia. The rarity of this disease does not enable prospective clinical trials to identify a better therapeutic strategy, which, at present, is based on clinicians' experience and on cooperation among them.

PP-10

A relapsed/refractory multiple myeloma patient with central nervous system involvement

R. Cifttciler[1], Ş. Ayar[2], K. Susesi[3], S. Aksu[1], Y. Buyukasık[1]
[1]*Hacettepe University, Faculty of Medicine, Department of Hematology;*
[2]*Hacettepe University, Faculty of Medicine, Department of Internal Medicine;*
[3]*Hacettepe University, Faculty of Medicine, Department of Pathology*

Objective: Neurological manifestations not infrequently complicate the course of patients with multiple myeloma (MM). They may occur in the setting of metabolic disorders such as hypercalcemia, uremia and hyperviscosity syndrome, spinal cord or nerve root compression and peripheral neuropathies related to amyloidosis or owing to toxicity of the administered treatment. Approximately 1% of MM patients develop central nervous system myeloma (CNS MM). A plasmablastic cytology and adverse cytogenetic abnormalities including IgH translocations and chromosome 13q deletions are associated with CNS MM. We present the clinical course of a 46-year-old woman with relapsed/refractory MM who had malignant plasma cells in the cerebrospinal fluid and 1.4 cm plasmacytoma in frontal lobe.
Case report: In this study, we present a patient with meningeal and CNS involvement in a relapse refractory multiple myeloma patient. She was diagnosed Ig A Kappa MM in 2015. Cytogenetic of the patients was 46XX. She received 8 courses of VCD as induction chemotherapy than she underwent autologous stem cell transplantation (ASCT) in 2016. After ASCT, she relapsed and she received lots of chemotherapy agent such as carfilzomibe, daratumumab, dexamethasone, lenalidomide, cyclophosphamide. She underwent second ASCT in 2017. She relapsed in 2019 again. In May 2019, VDTPACE (bortezomib, dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, and etoposide) chemotherapy was given to the patient who relapsed again. The patient was followed up in the hospital with neutropenia and thrombocytopenia after chemotherapy, while the patient complained of numbness in the jaw area. Cranial MRI was performed for this complaint. Cranial MRI revealed a dura-based 1.4 cm mass in the frontal lobe. CSF cytology of the patient was evaluated. Atypical plasma cell infiltration was observed. Patient received intrathecal chemotherapy. RT treatment was started.
Discussion: Meningeal and CNS involvement in MM is a rare complication. The prognosis of MM with CNS involvement is poor. The patients were reported in the literature as case reports or very small series. Because of the non-specificity of symptoms and signs of meningeal invasion in MM, an accurate diagnosis can be made by examination of CSF. The best treatment of meningeal myeloma has not been established. Intrathecal administration of methotrexate and craniospinal irradiation were performed in most cases. The life expectancy of patients with meningeal myeloma appears to be poor; treatment can temporarily palliate the central nervous system symptoms; however, it is still undetermined if it can prolong survival.
Conclusion: Although there are non-specific symptoms in patients with MM, imaging studies and CSF cytology should be performed for central nervous system involvement.

PP-11

Thrombotic thrombocytopenic purpura associated with pesticides: a report of four cases and literature review

V. Karakuş[1], E. Kaya[2], G. Zorlu Görgülügil[3], Y. Dere[3], E. Kurtoğlu[4]
[1]*Muğla Sıtkı Koçman University Education and Research Hospital, Department of Hematology;* [2]*Muğla Sıtkı Koçman University Educational and Research Hospital, Department of Physiology;* [3]*Antalya Research and Training Hospital, Department of Internal Medicine;* [4]*Antalya Research and Training Hospital, Department of Hematology and Therapeutic Apheresis Unit*

Objective: Thrombotic thrombocytopenic purpura (TTP) is a disease characterized by the presence of microangiopathic hemolytic anemia (MAHA) and thrombocytopenia, caused by the congenital or acquired decrease of the enzyme activity which degrades unusual large vWF multimers. There is no etiological cause in half of the acquired TTP cases. Herein we report four possible pesticide-related cases with decreased enzyme activity, an enzyme inhibitor shown, and typical clinical presentation.
Case report: The first case is a 20-year-old male patient with no medical history presented with a headache and weakness for 3 days. The patient used an antifungal pesticide containing pyrimethanil in order to kill wild herbs approximately one week prior to the diagnosis. The neurological examination was normal with no organomegaly. Acquired TTP was diagnosed, and therapeutic plasma exchange was initiated emergently. After the 6th cycle, the platelet count was >100,000/mm^3, and after 22 cycles (22nd day), the patient had a platelet count of >150,000/mm^3.
The second case is a 50-year-old male with no medical history or drug use presented with weakness and syncope. The patient mentioned the use of a single dose of an antifungal pesticide containing pyrimethanil in order to kill wild herbs approximately one week prior to the diagnosis. The patient had no neurological or systemic findings, except the fever of 39°C. The radiological examination of the central nervous system was done due to the syncope, and the results were normal. Therapeutic plasma exchange was performed based on the diagnosis of acquired TTP, and the platelet count reached >150,000/mm^3 after 5 cycles (5th day).
The third case is a 36-year-old male patient with no medical history, presented with abdominal pain and nausea for approximately one week. The patient mentioned the use of an antifungal pesticide containing 70% trichloromethylthio + 1.5% triadimenol in order to kill wild herbs approximately ten days prior to the diagnosis. He had few petechiaes on his lower extremities without any neurological or systemic abnormalities. The platelet count reached >150,000/mm^3 after 25 cycles (25th day) of therapeutic plasma exchange.
The fourth case is a 28-year-old female patient with no medical history presented with petechiae on her lower extremities, weakness, fever and a headache. The patient mentioned the use of a single dose of an antifungal pesticide containing copper hydroxide in order to kill wild herbs 8 days prior to the diagnosis. She had no physical, neurological or systemic abnormalities except a few petechial rashes. The platelet count reached >150,000/mm^3 after 6 cycles (6th day) of therapeutic plasma exchange.
Discussion: We used only plasma exchange in our patients without steroids, rituximab or any other immunosuppressives, and immediate clinical responses and complete responses were obtained within 30 days. All patients were in complete remission for 17–42 months.
Conclusion: In this study, we report four cases of possible pesticide-associated TTP showing immediate, complete and permanent responses to the plasma exchange, even though it is not reported in the literature.

PP-12

The role of hepatitis B-related chronic liver disease on the changes of iron parameters, B12 and folic acid levels

R. Cıftcıler[1], S. Ozenırler[2]
[1]*Hacettepe University, Faculty of Medicine, Department of Hematology;* [2]*Gazi University, Faculty of Medicine, Department of Gastrenterology*

Background: Chronic hepatitis B virus (HBV) infection influences 240 million people worldwide. Additionally, it can lead to chronic liver diseases including chronic hepatitis B (CHB), cirrhosis and hepatocellular carcinoma (HCC). Iron is very important particle for humans' biological functions and cellular biochemical processes including cell growth and proliferation. Both iron deficiency and iron overload cause significant and potentially fatal health risks, therefore the homeostasis of iron is tightly regulated. The liver has a significant function for iron homeostasis. Besides storing iron, the liver also produces transferrin which is an iron carrier protein in plasma and hepcidin which is a hormone regulating iron metabolism.
Aim: CHB patients are frequently referred to hematology outpatient clinic because of abnormal serum iron parameters. Therefore, this study aimed to evaluate changes serum iron parameters in patients with CHB and identify correlations between changes in iron metabolism and HBV-related liver injury.
Methodology: This study has been performed in a retrospective manner. Demographic data of the patients, fibrosis evaluation and laboratory studies

were obtained from hospital database. One hundred and twenty CHB patients who received a liver biopsy for evaluating fibrosis at Gazi University Hospital between the years of 2012 and 2016 were evaluated.

Results: One hundred and twenty patients with CHB and 60 healthy control subjects were included in this study. Distributions age (p=0.48) and gender (p=0.49) were similar between CHB patients and healthy controls. Serum iron (p=0.33), iron binding capacity (p=0.36), transferrin saturation (p=0.17), B12 level (p=0.48) and folic acid level (p=0.23) were similar between CHB patients and healthy control groups. However, ferritin level (p=0.04) was statistically significant higher in CHB patients than in healthy controls. For subgroup analyses all biopsies were assessed and scored according to the Ishak's scoring in CHB patients. Fibrosis stage was graded up to 6: F0, no fibrosis and F6, cirrhosis. A significant positive relationship was seen between fibrosis stage and ferritin level (p<0.001), also fibrosis stage and transferrin saturation (p<0.001). However, there was no statistically significant relationship between fibrosis stage and iron (p=0.71), additionally fibrosis stage and iron binding capacity (p=0.24).

Conclusion: In conclusion, there is a strong relationship between severity of parenchymal liver disease and serum ferritin level and transferrin saturation. Patients with cirrhosis (F6) frequently have increased TS and ferritin levels. In many advanced cirrhosis cases, TS and ferritin were simultaneously elevated, which may lead to suspicion of iron overload. These properties may be beneficial in the interpretation of serum iron test results in patients with CHB as well as patients with liver disease. Additionally, there was no significant relationship between b12 and folic acid levels and fibrosis stage.

PP-13
A case report of carfilzomib-induced hepatotoxicity

M. Ulukoylu Menguc, A. Geduk, S. Mersın, S. Unal, M. Polat, K. Aygun, P. Tarkun, Ö. Mehtap, A. Hacıhanefıoglu
Kocaeli University Hematology

Background: Carfilzomib, an irreversible proteasome inhibitor, entered clinical development in 2005 as a potential treatment for MM. Carfilzomib has a high specificity for the proteasome with minimal activity against a wide range of other cellular targets. Carfilzomib induces a dose-dependent suppression of proteasome activity in all tissues examined except the brain, suggesting that the compound does not readily cross the blood–brain barrier. Carfilzomib has rapid clearance with an elimination half-life of less than 30 min and a clearance higher than liver blood flow, which suggests there are multiple clearance pathways. CFZ is administered intravenously. If signs of dose intolerance occur, a dose reduction down to 20 mg/m^2 or an extension of infusion time up to 30 minutes can be considered. CFZ penetrates all tissues but the brain extensively. It is largely metabolized extrahepatically and is rapidly cleared from the circulation by biliary and renal excretion (t1/2 15–30 min): less than 1% is excreted intact. Unlike BTZ, CFZ is not primarily metabolized by hepatic cytochrome P450 and therefore plasma levels are minimally dependent on liver function and concomitant medication.

Case report: 49-year-old female patient was diagnosed IgG lambda multiple myeloma, ISS stage 1 in 2009. After 4 courses of VAD, 8 courses of VD, 2 courses of thalidomide she had tandem autologous bone marrow transplantation in 2012. Following transplantation she had lenalidomide maintenance for 14 months and received 6 courses of VD because of progression with a very good partial response. At that time she had no matched or unmatched donor and was followed without treatment. 14 months later she had a nonaggressive relapse and was restarted lenalidomide 15 mg combined with dexamethasone weekly 40 mg. Lenalidomide was stopped at the end of course 4 because of grade 3 cytopenias and grade 3–4 diarrhea. In July 2018 as having monoclonal IgG L band and anemia carfilzomib dexamethasone course started. First course included carfilzomib 20 mg/m^2 was increased to 27 mg/m^2 on days 8, 9, 15, 16 every 21 days with asymptomatic status and normal laboratory tests. At the beginning of third cycle she admitted with transaminases elevated by 4–5 factor with a minimal response. There was no concomitant medication or herbals except with dexamethasone. She had no history of hypotension or hypovolemia. Abdomen ultrasonography revealed normal sonographic findings with normal viral serology including viral hepatitis (A, B and C), cytomegalovirus IgM, Epstein-Barr viral capsid antigen IgM, Herpes simplex IgM which were all negative. We thought toxic hepatitis due to carfilzomib and the drug was stopped. Liver function test improved after discontinuation and normalized in two weeks.

Discussion: In this article we report a 59-year-old heavily pretreated female patient having liver toxicity after two courses of carfilzomib treatment. Liver function test improved after discontinuation and normalized in 2 weeks.

Conclusion: During carfilzomib treatment liver functions should be monitored.

PP-14
POEMS syndrome treated with autologous hematopoietic stem cell transplantation

E. Abdullayev[1], E. Abdullayev[2], H. Baurmann[1], C. Eimermacher[1], B. Glass[1]
[1]*Helios Klinikum Berlin Buch, Department of Stem Cell Transplantation, Hematology, Oncology and Palliative Medicine, Berlin, Germany;* [2]*Nakhchivan Military Hospital, Department of Intensive Care Unit, Nakhchivan, Azerbaijan*

Background: Polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes (POEMS) syndrome is a rare systemic pathology of paraneoplastic origin that is associated with plasma cell dyscrasia. It is characterized by the presence of sensorimotor polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes, and other systemic manifestations. The pathogenesis of the syndrome is unknown but over-production of vascular endothelial growth factor is probably responsible for most of the more characteristic symptoms. There is no standard treatment for POEMS syndrome and no randomized controlled clinical trials of treatment exist in the available literature. High-dose melphalan with autologous hematopoietic stem cell transplantation should be considered for younger patients with widespread osteosclerotic lesions, and for patients with rapidly progressive neuropathy.

Case report: This is the case of a 36-year-old male patient, a butcher, with a deep vein thrombosis of the proximal femoral vein superficialis to the distal lower leg veins on the left, who was hospitalized with pain in the left leg increasing numbness and weakness of the feet as well as erectile dysfunction. Already in May, the patient also noticed soft mass on the skull. Blood analysis discovered a slight increase in the lambda light chain fraction, Vitamin D3 deficiency A computerized tomography (CT) scan of the full-body was made, which substantiated large osteolysis of the calf of the skull left high parietal, evidence of a brain-splitting plasmacell tumor on the left parietal occipital with suspected dural and glial infiltration and presence of splenomegaly. In transthoracic echocardiography, the left ventricle was somewhat thickened. Here cardio MRI was performed, which showed no cardiac amyloidosis. A Sonography of the deep veins of the legs showed no signs of persistent thrombosis. A neurophysical examination was performed, which verified the existence of distal sensorimotor axonal neuropathy. An immunofixation test confirmed lambda-IgG monoclonal bands. In the present case the biopsy of bone marrow was negative. There was no evidence of Bence-Jones proteins in the urine. b2-microglobulin was normal. The soft mass on the skull was operated. Histologically, here, a manifestation of a plasmacytoma with light chain restriction can be seen. Once the diagnosis of POEMS had been established, the patient was treated with local Radiation of the skull. The patient has received 4 cycles of Lenalidomide and Dexamethasone chemotherapy. After 2 cycles of chemotherapy, stem cell apheresis was performed. Here a total of 5 million CD34 positive cells per kg of body size were collected. Chemotherapy showed a significant improvement in neurological symptomatology. Furthermore, we decide on high-dose chemotherapy with melphalan I.V. (200 mg/m2), followed by autologous hematopoietic stem cells transplantation (HSCT), as the patient fulfilled the requirements for this procedure six months after the procedure, the patient showed a notable clinical improvement; the peripheral neuropathy had disappeared (normalization in neurophysical assessment). In time, the rest of the clinical and analytical manifestations went into remission, and this included the absence of the monoclonal component as shown by Immunofixation testing.

Conclusion: The present case report, which endorses HSCT in combination with an intensive chemotherapy regimen as one of the most active and effective therapies for the disseminated form of POEMS syndrome.

PP-15

CD34+ selected stem cell boost for CMV induced poor graft function after allogeneic stem cell transplantation

E. Abdullayev[1], E. Abdullayev[2], H. Baurmann[1], S. Fuhrmann[1], B. Glass[1]
[1]Helios Klinikum Berlin Buch, Department of Stem Cell Transplantation, Hematology, Oncology and Palliative Medicine, Berlin, Germany; [2]Nakhchivan Military Hospital, Department of Intensive Care Unit, Nakhchivan, Aserbaijan

Case report: This is the case of a 43-year-old male patient, with a pro-B-ALL (high risk). Who have got HYPERCVAD and Prophase and Consolidation II chemotherapy according to GMALL protocol and Blinatumomab. He was transplanted with MUD (9/10), ABO compatible. Conditioning was according to the myeloablative standard protocol (with TBI/cyclophosphamide/ATG). The patient was in with trilineage cytopenia until day +28 after Transplantation. During the prolonged aplasia and also partial reconstitution of granulopoiesis patient repeatedly fever. Only once detected skin germs in blood cultures (Staph. epid. and Corynebacterium). We, therefore, treated empirically. At continuous positivity of Candida-Ag and unique positive Aspergillus-Ag in serum. Due to pneumonic infiltrates, Anidulafungin prophylaxis (for graft failure and general aplasia) was switched to Caspofungin and Voriconazole later Posaconazole. At the time of graft failure, CMV was detected in both bone marrow and pharyngeal fluid. In severe, previously confirmed HSV mucositis with deep ulcerations of the tongue and progression under therapeutic doses of Acyclovir, we changed the antiviral therapy to Foscavir, which improved the mucositis very slowly and the patient achieved at least a partial reconstitution of granulopoiesis, so we consider CMV to be of course causative for graft failure. In the course of development, patients with sustained lymphopenia with helper counts of less than 50/µl still develop BK virus-associated hemorrhagic cystitis, which requires a continuous flow irrigation middle flushing catheter needed. As a maintenance therapy for the virus-induced mucositis and the best possible treatment of BK virus, antiviral treatment was switched to Cidofovir. The only day +46 after more than 2 weeks of G-CSF administration and treatment of a CMV reactivation in the bone marrow with Foscavir, we once observe a granulocyte count continuously above 500/µl, from day +48 the granulocytes were above 1000/µl. Stimulation with G-CSF was carried out every second and third day in the case of sloping granulocytes. By day +88, no platelet or erythrocyte Engraftment could be achieved. A donor chimaerism was on day +14 80%, on day +31 97%. on day 81 99.3% with receiver signal. The delayed Entgrafment and persistent graft dysfunction were assessed on day +26 with evidence of CMV in the PCR as transplant failure in 1-Ag MM, possibly in the absence of enhancing T-cells after high ATG levels with intensive pre-treatment and additional hematotoxicity effect of CMV. Due to the MRD negativity before and after transplantation, there is no suspicion of the persistence of ALL as the cause of the poor transplant function. A patient has been given day +95 by the same donor stem cell boost 7.9×10^6 CD34+ cells. Cidofovir maintenance therapy could not be administered due to renal insufficiency, despite renewed evidence of HSV in the rinsing lavage and also a renewed CMV reactivation. We decide for the time being on an acyclovir treatment with the option to switch to Vangancyclovir after growth of the stem cell boost. During 2 monthly outpatients, we see the bone marrow completely reconstituted, no CMV reactivation detectable again.

PP-16

Gastrointestinal plasmoblastic lymphoma associated with Wiskott-Aldrich syndrome: a case report

A. Ünal, S. Çelik, Z. Güven, L. Kaynar, B. Eser, M. Çetin
Erciyes University, Faculty of Medicine, Hematology Department

Introduction: Plasmablastic lymphoma (PBL) is a rare and aggressive subtype of non-Hodgkin lymphoma that commonly occurs in human immunodeficiency virus (HIV)-positive individuals. But also PBL can be seen in patients with other immunodeficiencies as well as in immunocompetent individuals. Wiskott-Aldrich syndrome (WAS) is a primary immunodeficiency disorder with X-linked recessive transmission that being susceptible to infections and also reduced ability to form blood clots. We report a case of gastrointestinal PBL in a 28-year-old male patient who had been diagnosed with WAS for 12 years.

Case report: He was admitted to our clinic with hematemesis and melena complaints and endoscopy was performed. A 5×4 cm mass was observed in the gastric antrum and biopsy was reported plasma cell dyscrasias with kappa monoclonal. PET/CT was performed: Bilateral paraaortic area, common iliac chain, internal and external iliac chain and bilateral inguinal area were observed in multiple lymph nodes with moderate-dense hypermetabolic activity of 35×25 mm in size, and intense hypermetabolic activity in lung, stomach and spleen were seen. These findings were primarily evaluated as nodal and extranodal involvement of malignant lymphoproliferative processes (lymphoma?). Physical examination revealed ascites, hepatosplenomegaly and hyperpigmentation under both knees. Ascites sampling showed diffuse plasmocytic cells, and flowcytometry showed peritoneal involvement of: CD38+, CD138+, CD56–, CD19–. Bronchoscopy was performed and atypical plasma cell proliferation was observed. Anti-HIV was negative. We started Bortezomib, Cyclophosphamide and Dexamethasone treatment.

Discussion: PBL is a subtype of diffuse large B-cell lymphoma usually seen in HIV-positive patients. In a review of 590 cases by Castillo et al., 28% of PBL patients were HIV-negative. However, in all cases with PBL, as in our patient, there is an immunosuppressed situation. Again in the same review the sex distribution shows a male predominance (75%). In PBL, the most common site of involvement, regardless of whether HIV-positive or negative, is oral (48% and 40%) and gastrointestinal (12% and 21%) respectively. However, involvement can be seen almost everywhere. PBL is a high-grade neoplasm with cytomorphologic features such as large immunoblasts or large plasma cells that express plasma cell markers and lack B-cell markers. The diagnosis of PBL is challenging because it has features that overlap with those of myeloma and with lymphomas that have plasmablastic morphology. The immunophenotype is similar to that in plasma cell neoplasms, positive for CD79a, IRF-4/MUM-1, BLIMP-1, CD38, and CD138. The neoplastic cells are negative for B-cell markers CD19, CD20, and PAX-5; however, a subset may be dim positive for CD45. Some cases express T-cell markers CD2 or CD4. Epstein–Barr virus infection and MYC rearrangements are frequently observed. Treatment of PBL is challenging because of the lack of established treatment and poor outcomes, with median survival times shorter than one year.

Conclusion: PBL is a very rare disease and it is quite difficult to diagnose because it contains different components. PBL should be considered in immunosuppressive patients that have negative B cell markers and positive plasma cell markers.

PP-17

Case of atrial fibrillation secondary to ibrutinib and resulting in death

M. Reis Aras, M. Albayrak, B. Sağlam, S. Maral, H. Afacan Öztürk, A. Yıldız
University of Health Sciences Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital, Department of Hematology

Introduction: Chronic lymphocytic leukemia (CLL) is the most common leukemia in adults. The most common genetic abnormality is del 13q and is found in about half of patients. 17p deletions found in 5–8% of cases. Treatment is indicated in patients in whom marked bone marrow suppression symptoms (anemia or thrombocytopenia) and disease-related symptoms (e.g., B symptoms or discomfort caused by large nodal masses) develop. In recent years, new kinase inhibitors (ibrutinib, idelalisib) and Bcl-2 inhibitors (venetoclax) have also been used for the treatment of CLL. Ibrutinib is an oral Bruton kinase inhibitor. It is usually a well-tolerated treatment option by patients. However, some side effects may occur. Most often diarrhea, upper respiratory tract infection, bleeding, loss of appetite and cardiac side effects.

Case report: A 63-year-old female patient diagnosed with CLL in 1999 and followed for 19 years without treatment. After B symptoms appeared and splenomegaly was detected; rituximab, fludarabine, cyclophosphamide

(R-FC) chemotherapy protocol was initiated. Echocardiography (ECO) and electrocardiogram (ECG) performed before chemotherapy, they were within normal limits. R-FC chemotherapy protocol was completed in 6 cycles and evaluation tests were interpreted as complete remission. Six months after the completion of six cycles of R-FC treatment, chest X-ray showed infiltration of the basal part of the right lung and thoracic tomography was performed. EBUS (endobronchial ultrasonography) was performed for the existing lung lesion and fine needle aspiration biopsy (FNAB) was performed in the procedure. Cytological results of FNAB samples were reported compatible with CLL. The patient with lung involvement, lymphocytosis (leukocyte value: 8.5×10^3/µl lymphocyte: 4.5×10^3/µl hemoglobin: 11.1 g/dl platelet: 111,000) and B symptoms was considered to be recurrent CLL. Upon the positive 17p deletion of the patient, ibrutinib was applied. Ibrutinib was started at a dose of 140 mg tablets 1×3. Ibrutinibe was discontinued upon the development of pneumonia under treatment, and the drug was continued as the infection regressed. The patient developed pneumonia again during the follow-up and was admitted to the hospital. In physical examination, pretibial 3+ edema and right heart failure findings revealed. Atrial fibrillation (AF) was detected in her ECG. The patient consulted to cardiology. Metoprolol, LMWH, ramipril and aldactone were added to the treatment with the recommendation of cardiology. Ultrafiltration was performed with the suggestion of nephrology. The patient's general condition was poor and she was intubated due to sudden respiratory distress. The patient did not respond to the treatments and died.

Discussion: The pathogenesis of arrhythmias secondary to ibritunib is unclear. Concomitant use of ibrutinib and warfarin should be avoided because of the risk of bleeding. In extensive studies in patients with atrial fibrillation, reduced dose direct thrombin inhibitors or factor Xa inhibitors have been shown to have warfarin-like protective effects against stroke.

Conclusion: In view of all these findings, long-term use of NOACs with ibrutinib, may be considered after the the safety of NOACs is confirmed.

PP-18

A rare association, myelofibrosis secondary to essential thrombocytosis and monoclonal gammopathy of undetermined significance

M. Reis Aras, M. Albayrak, S. Maral, P. Cömert, A. Yıldız, B. Sağlam
University of Health Sciences Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital, Department of Hematology

Introduction: Monoclonal gammopathy of undetermined significance(MGUS) is an asymptomatic and premalignant clonal plasma cell disease. It is characterized by serum M protein concentration <3 g/dL, <10% plasma cell detection in the bone marrow and absence of CRAB findings (hypercalcemia, anemia, renal failure, lytic bone lesions). Essential thrombocytosis (ET) is a chronic myeloproliferative disease characterized by clonal proliferation of hematopoietic cells. Approximately 55% of patients have positive JAK2 mutation. Comprehensive studies have shown that patients with ET may develop post-ET myelofibrosis at a rate of 3.9% over a 10-year period.

Case report: A 55-year-old female patient diagnosed with JAK-2 negative ET in 2004 in another hospital. There was started anagralide treatment one year after the diagnosis. Anemia developed in the tenth year after diagnosis of essential thrombocytosis. She was examined about anemia; Ig G lambda monoclonal band in serum immunoelectrophoresis and gamma peak in protein electrophoresis were revealed. In bone marrow biopsy plasma cell ratio was <10%. CRAB findings were negative. According to examination results the diagnosis was MGUS. In the second year of ET and MGUS diagnosis, bone marrow biopsy was performed because worsening of anemia. Bone marrow biopsy was found to be compatible with myelofibrosis; anagralide discontinued, hydroxyurea and acetylsalicylic acid added to treatment. On admission to our hematology department in 2017, she was taking hydroxyurea 500 mg/day and acetylsalicylic acid 100 mg/day. She had any comorbid risk factors. On her treatment regimen acetylsalicylic acid was continued but hydroxyurea was discontinued. In the genetic analysis JAK-2 mutation, JAK-2 exon 12, CALR, MPL gene w515L/K, BCR-ABL mutation were reported as negative. In January 2019 bone marrow biopsy performed for deep cytopenia. It was reported as "grade III/III diffuse fibrosis, presence of 5–7% plasma cells, hypercellular bone marrow showing myeloid/megakaryocytic serial proliferation". Abdominal ultrasonography performed, splenic long axis revealed 180 mm. The patient was followed-up in our clinic with the diagnosis of MGUS and post-ET myelofibrosis. In February 2019, ruxolitinib was started at a dose of 15 mg twice daily. Because of insufficient response in the sixth month of ruxolitinib treatment, HLA tissue groups were studied in the patient and her siblings. As a sibling is a fully compatible donor, preparations were started for allogeneic bone marrow transplantation.

Discussion: At present, management strategies are treating the MPN and regularly monitoring the MGUS for transformation to multiple myeloma.

Conclusion: Agents such as thalidomide, lenalidomide and pomalidomide have an effect on both myeloproliferative disease and myeloma. It is also of interest whether JAK inhibitors such as ruxolitinib, which reduce the inflammatory cytokine signal (including IL-6), will have an antimyeloma effect in this association. Further studies are needed to evaluate optimal treatment options in this patient population.

PP-19

Evaluation of the prevalence of hepatitis B and C in patients with lymphoma

M. Togun[1], M. Buyuksimsek[2]
[1]*Cukurova University Faculty of Medicine Dep of Internal Medicine;* [2]*Cukurova University Faculty of Medicine Dep of Medical Oncology*

Objective: Hepatitis reactivation during chemotherapy is a major problem in lymphoma patients. Despite the increase in hepatitis vaccination and prevention programs, the prevalence of hepatitis B and hepatitis C in developing countries is still well above the targeted levels. We aimed to investigate the prevalence of hepatitis B and hepatitis C in lymphoma patients treated in our center.

Methodology: Of the 240 NHL patients, 147 (61%) were male and 93 (39%) were female. The mean age of female patients was 52.3 years and the mean age of male patients was 54.1 years. 142 of our patients were from DLBCL, 38 were follicular lymphoma, 27 were mantle cell lymphoma, 13 were small lymphocytic lymphoma, 8 were extra nodal marginal zone lefoma, 7 were burkit lymphoma, 5 were primary mediastinal lenfoma subtype. In 21 (8.7%) of the NHL patients, Hbsag antigen was positive (10 of them with DLBCL, 5 with Follicular Lymphoma, 3 with mantle cell lymphoma, 2 with extra nodal marginal zone lymphoma, 1 with Burkit lymphoma). Anti-HCV positivity was detected in 9 patients (3.7%) (7 of them had DBBHL, 1 had extra nodal marginal zone lymphoma and 1 had mantle cell lymphoma). In 79 (33%) patients, Hbsag (–), antiHbs (+), anti-Hbc (+) were detected and evaluated as previous hepatitis B infection. The files of non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma (HL) patients treated in our center between 2012–2018 were retrospectively reviewed. HBsAg, AntiHbs, AntiHbc, Anti-HCV parameters of the patients were evaluated.

Results: Of the 110 HL patients, 64 (58%) were male and 46 (42%) were female. The mean age of female patients was 36.4 years and the mean age of men was 39.2 years. Hbsag (+) was detected in 10 (9.1%), Anti-HCV (+) in 3 (2.7%) and antiHbc (+) in 29 (26%) of the patients.

Conclusion: In a study conducted in persons over the age of 18 in 2009, HBsAg positivity was found to be 4% and antiHBc positivity was found to be 30.6% in our country. In a study published in 2012, it was reported that the frequency of anti-HCV in the study participants was between 0.5 and 1% [1]. In our study, HBsAg positivity was 8.7%, antiHBc positivity was 33% and anti-HCV positivity was found to be 3.7%. According to the data of our country higher positivity was determined. This may have been due to the fact that hepatitis can cause lymphoma on their own. In HL patients, 9.1% HBsAg positivity, 26% antiHBc positivity, 2.7% anti-HCV positivity was detected. Hepatitis B and C positivity in our region poses an important problem. All patients should undergo these tests before the chemotherapy and positive ones should be treated. Necessary information about vaccination and prevention methods should be provided.

Reference

[1] Tozun N, Ozdogan O, Cakaloglu Y, et al. Seroprevalence of hepatitis B and C virus infections and risk factors in Turkey: a fieldwork TURHEP study. Clin Microbiol Infect 2015;21:1020–6.

PP-20

Long-time overlooked blastic plasmacytoid dendritic cell neoplasm evolving into multiple organ involvement presentation

Z. Istemihan[1], S. Ozkan[2], O. Dogan[3], I. Yonal-Hindilerden[2], S. Kalayoglu-Besisik[2], S. Kalayoglu-Besısık[2]
[1]Istanbul University, Istanbul Faculty of Medicine, Departmen of Internal Medicine, Istanbul, Turkey; [2]Istanbul University, Istanbul Faculty of Medicine, Departmen of Internal Medicine, Division of Hematology, Istanbul, Turkey; [3]Istanbul University, Istanbul Faculty of Medicine, Departmen of Pathology, Istanbul, Turkey

Background: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is an aggressive and rare neoplasm. It often presents with skin involvement subsequent or simultaneous spread to bone marrow and peripheral blood. BPDCN is classified as a member of the AML/related family of neoplasms by the World Health Organization (WHO) in 2008. Blastic cells are of medium size, with narrow and without granular cytoplasm and are defined with immunophenotypic triad that helps to identify the disease: CD4+CD56+CD123+. BPDCN can occur at any age but is most common in the elderly and male sex. The prognosis of BPDCN is poor with a median overall survival (OS) of ~12–14 months.
Case report: A 29-years-old male patient presented with multiple erythematous skin lesions, with plaque and nodule appearance, big necrotic ulcerated mass lesion on the anterior site of the left lower limb and bilateral ecchymotic swelling of eyelids. He had a history of steroid-containing systemic treatment for the left leg lesion 6 months ago which resulted to disappearance of the lesion. He denied sweating, weight loss and fever. Physical examination revealed mild paleness in addition to the skin findings. No spleen, liver, lymphadenomegaly were palpable. Blood chemistry and hemogram were within normal limits. Bone scintigraphy revealed no bone involvement around ulcerated mass lesion but bilateral involvement at lower part of femur and upper part of tibia. PET-CT showed skin lesions involving sites and bone activities consistent with bone scan result. Peripheral blood and bone marrow showed atypical cells in varying size, with narrow, granule-free, budding cytoplasm, and inconspicuous nucleolus. By flow-cytometric analysis the cells were found CD45, HLA DR, CD4, CD33, CD38 and anti-lambda positive but CD3 and CD34 negative. No definitive diagnosis was made. Skin biopsy was performed. Histological examination showed CD4, CD56, CD123, CD33, CD68 positive cell infiltration which were CD3 and CD20 negative. BPDCN was diagnosed. No karyotypic abnormality was detected. PCR studies for AML and ALL-related recurrent cytogenetic abnormalities were found to be negative. ALL like treatment was chosen. HyperCVAD protocol was started. All skin lesions disappeared during the first week, including the necrotic lesion. He underwent in remission allogeneic peripheral stem cell transplantation from his HLA identical brother following myeloablative conditioning regimen. He is still alive and in remission for 3 years.
Discussion: BPDCN can be recognized by multiorgan involvement. Generally, the skin is the first affected site. Involvement of bone marrow, peripheral blood, and lymph node can be seen as bystanding or evolving.
Conclusion: At diagnosis, bone marrow should be routine investigated even without cytopenia. We think also whole-body screening is important to evaluate the disease extent and monitoring the response status since organ and tissue involvement can be asymptomatic. However, in our case, bone involvement was asymptomatic. The treatment recommendation for the disease is systemic and primarily with ALL like treatment protocols followed by allogeneic transplantation in suitable patients.

PP-21

Suppression of miRNA-223 in adult acute myeloid leukemia is associated with adverse cytogenetic profile and undifferentiated blast morphology

G. Elyamany[1], O. Alsuhaıbanı[1], H. Aljasem[2], S. Alotaıbı[2], A. Mansoor[1]
[1]Department of Central Military Laboratory and Blood Bank, Prince Sultan Military Medical City (PSMMC), Riyadh, SA; [2]Department of Hematopoietic Stem Cell Transplantation and Adult Clinical Hematology, Prince Sultan Military Medical City, Riyadh, SA

Objective: MicroRNAs (miRNA) signatures are shown to exert an important role in patho-biology of acute myeloid Leukemia (AML). miR-223, is expressed at low levels in hematopoietic stem cells, but its expression increases dramatically during granulocytic differentiation. miR-223 exhibits its antiproliferative effects by targeting the transcription factors like MEF2C, that is up-regulated in leukemic monocyte. In this study, we evaluated the expression of microRNA-223 in a large cohort of AML pts. and correlated it with pattern of granulocytic differentiation. We also explored the association of microRNA-223 expression with chromosomal abnormalities as well as with overall survival.
Methodology: Diagnosis/classification (FAB, WHO 2008) was based on morphology, flow-cytometry and conventional cytogenetics/FISH studies. Diagnostic bone marrow biopsy tissue (FFPE) was utilized to extract microRNA. miScript SYBR Green PCR Kit was used to amplify the target (miR-223). Normal BM samples and peripheral blood mononuclear cells were used as normal controls. ddCt algorithm was used to analyze relative changes in gene expression. SPSS (version 20.0) was used for statistical analysis.
Results: 104 patients (18–89 years, mean 55 years, median 59 years, 67 men and 37 women, M:F 1.8:1) were included. Morphologically patients were classified as, M0/M1 (21/104; 20%); M2 (13/104, 13%); M3 (11/104, 11%); M4/M5 (26/104, 25%); M6/M7 (7/104, 7%) and others (26/104, 25%). Diploid karyotype was seen in 38/104 (37%) while aneuploidy in 66/104(63%). miR-223 expression was higher (>1.2 fold) in only 28/104 (27%). miR-223 expression was higher in AML with diploid karyotype, compared to AML with aneuploidy (37% vs. 16%) ($p<0.0194$). Higher expression of miR-223 was noted most frequently in AML with differentiation (FAB-M2) (11/13; 85%) compared to M0/M1 (5%; $p<0.0001$); M3 (0%; $p<0.0001$); M4/M5 (17%; $p<0.0004$); AML-MDS (27%; $p<0.0105$). miR-223 showed no correlation with over-all survival with either normal vs. abnormal cytogenetic sub-groups or any FAB subtypes.
Conclusion: Suppression of miRNA-223 in de-novo adult AML pts. is related with undifferentiated blast morphology. AML associated with differentiation have shown high expression of miRNA-223. Higher miRNA-223 expression is related with diploid karyotype. Suppression of miRNA-223 levels are linked with adverse cytogenetic risk profile. miRNA-223 expression patterns was unrelated with overall survival.

PP-22

The role of ETS-1 transcription factor in the pathogenesis of chronic lymphocytic leukemia

V. Karakuş[1], E. Kaya[2]
[1]Mugla Sitki Kocman University Resarch and Education Hospital, Department of Hematology, Muğla, Turkey,; [2]Muğla Sıtkı Koçman University, Faculty of Medicine, Department of Physiology, Muğla, Turkey

Objective: The first members of the ETS family of transcription factors are ETS-1 and ETS-2. They are cloned as human homologues of the v-ETS protooncogene of avian retrovirus E26. In humans, ETS-1 is identified on chromosome 11. ETS factors are divided into subgroups according to sequence similarities in the ETS domain, the presence of shared and protected areas by some ETS factors that function in hetero or homodimerizations. Target genes include transcription factors associated with apoptosis, differentiation, proliferation, angiogenesis, invasion, and metastasis. We aimed to demonstrate the role of ETS-1, which has been mapped on the 11q chromosome, often exposed to genomic deviations in mature lymphoid cancers, the expression of ETS-1 and the pathogenesis of mature lymphoid cancer.
Methodology: A total of 50 cases were included in the study. In addition to the demographic data, the clinical picture, the stage of the disease, the

pattern of the infiltration in the bone marrow, molecular examination results, hematologic parameters at the time of diagnosis were noted. Sections of 3–4 μm thickness were prepared for ETS-1 immunohistochemical staining from paraffin blocks of bone marrow biopsies of patients. The stained sections were examined with Olympus BX46 trinocular microscope. Statistical analysis of the data was performed with SPSSv20.

Results: 59 patients met the inclusion criteria and the mean age was 69.04. Among the clinical data, lymphadenopathy was present in 33 patients, splenomegaly in 24 patients and hepatomegaly in 8 patients. FISH examination was performed in 18 patients and 7 of these patients were found to have FISH (–) (11.86%). The most common mutations in FISH (+) patients were del 13q14.3 (n=5) and tri 12 (n=5). Del 11q22.3, del 13q3.4 and t (11; 14) (q13; q32) were detected in 2 patients (3.39%) and one of the patients had 3 FISH abnormalities together. According to the immunohistochemical staining, in only two cases (3.39%) showing nodular and interstitial patterns together Ets-1 expression are found to be weak. 57 cases (96.61%) were interpreted as ETS-1 (–).

Conclusion: In the rats overexpressing TCL 1, B-CLL is developed and this development is seen in humans as well. These results demonstrated the importance of TCL-1 deregulation in the pathogenesis of B CLL. TCL-1 interacts with the p300 protein. One of the best studied pathways containing P300 protein is activator protein 1 (AP-1) dependent transcription. The best-known AP-1 complexes are c-Jun, c-Fos, other Jun proteins, fos proteins. JunB deficiency plays a role in the pathogenesis of B cell leukemia. Mutations in ETS-1 have been shown to reduce JunB promoter activity but mutations in the AP-1 region do not reduce JunB promoter activity. These results show that the ETS-1 binding site is responsible for JunB promoter activity. This study demonstrated that in CLL, ETS-1 levels decrease and may have an important role in pathogenesis. This is a pilot study to plan new studies to elucidate the expression of ETS-1 in the hematopoietic stem cell which will shed light on the origin of CLL and the effect of genetic polymorphisms in ETS-1 on the development of the disease.

PP-23

LYN and HDX gene mutations in patients with acute promyelocytic leukemia

E. Gheisari[1], H. Pashaiefar[2], M. Yaghmaie[2], S. Mousavi[2], N. Gerayeli[2], K. Alimoghaddam[2], A. Ghavamzadeh[2]
[1]Faculty of Basic science, Department of Biology, Islamic Azad University east Tehran branch, Tehran, Iran; [2]Hematology, Oncology and Stem Cell Transplantation Research Center, Tehran University of Medical Sciences, Tehran, Iran

Objective: The t(15;17) translocation generating a PML/RARA fusion gene is necessary, but not sufficient, in the trigger and development of acute promyelocytic leukemia (APL). It is now widely accepted that secondary genetic lesions are required for the APL development in up to 40% of these cases. Divergent homeobox gene HDX and tyrosine kinase LYN play strong potential roles in leukemogenesis.

Methodology: Here we performed mutational analysis in 80 APL patients by Sanger sequencing in HDX and LYN genes to evaluate the possible roles of these mutations as additional genetic abnormalities that cooperate with PML/RARA in APL development. All the exons encoding domains with well-defined functions as well as intron-exon boundary regions were sequenced (exons 2, 5 and 6 of HDX gene and exons 8–13 of LYN gene).

Results: We identified 4 missense substitutions in HDX gene including A473V, S460G, D446E, and L450I and 2 missense substitutions in LYN gene including L379P and T310N. Comparing of the HDX and LYN sequence in the paired APL patients in remission we could identify that these mutations were APL-specific genetic variants.

Conclusion: Our findings suggest that the mutations in the LYN and HDX may be serve as cooperating events in APL development.

PP-24

Combination therapy of pegylated interferon alpha 2a and ruxolitinib in myelofibrosis: a case report

F. Hindilerden, I. Demiriz
S. B. Ü Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi Hematoloji Kliniği

Background: Ruxolitinib, a potent anti-inflammatory agent, has demonstrated benefit in myelofibrosis (MF) and polycythemia vera. Interferon alpha reduces elevated blood cell counts and splenomegaly in patients with myeloproliferative neoplasms and may restore polyclonal hematopoiesis. Combination therapy with these two agents may be more efficacious than monotherapy with either, potentially improving tolerability of both drugs as well.

Case report: A 55-year-old female was referred to our clinic for the underlying etiology of noncirrhotic portal hypertension. Abdominal CT angiography showed portal and superior mesenteric vein thrombosis in the presence of splenomegaly measuring 200 mm on longitudinal axis. Collateral veins were evident at the esophago-gastric junction, the splenic hilus and around the portal vein. Her complete blood count (CBC) was as follows: Leucocyte: 6400 Hgb: 12.6 PLT: 484000. JAK 2 mutation was positive. Bone marrow biopsy was compatible with primary MF. Hydroxyurea and oral anticoagulation with warfarin were started. Also, she underwent band ligation for eradication of esophageal varices. Seven months under hydroxyurea (1000 mg/day) and appropriate anticoagulation, spleen size was found to be moderately decreased measuring 180 mm on longitudinal axis. Yet, the patient had to undergo band ligation due to development of grade 3 esophageal varices. Although hydroxyurea was increased to the maximum dose of 2 gr/day, spleen size remained at 180 cm on longitudinal axis and she suffered from repeated episodes of esophageal varices. Ruxolitinib 2×20 mg was initiated. At the start of ruxolitinib, her CBC was as follows: Leucocyte:3400 Hgb:13.7 PLT: 252000. Six months after initiation of ruxolitinib, spleen size decreased to 150 mm and no episodes of esophageal variceal bleeding were reported. Yet by the 10th month, the patient developed pancytopenia with the following CBC: Leucocyte: 2500 Hgb: 8.6 PLT: 152000. Iron deficiency was excluded. Ruxolitinib was decreased to a dose of 15 mg/day. Yet, cytopenias persisted with the following CBC: Leucocyte: 2400 Hgb: 8.4 PLT: 101000 and the spleen size increased moderately to a size of 170 mm. To maintain the spleen response and concomitantly to prevent the worsening of cytopenias, pegylated interferon α2 (PEG-IFNα2) 135 μg/3 weeks SC was added and ruxolitinib was decreased to 10 mg/day. Five months under this triple combination, spleen size decreased to 150 mm and the cytopenias improved with the following CBC: Leucocyte: 4000 Hgb: 9.9 PLT: 142000. Also, no new esophageal variceal bleeding episodes attributed to portal venous thrombosis were encountered.

Conclusion: Our experience with the combination of PEG-IFNα2 and ruxolitinib are in line with the findings suggesting that chemotherapy with low-dose PEG-IFNα2 and ruxolitinib is feasible and efficacious in patients with low-/intermediate-risk MF. The combination treatment should be considered in MF patients, who experience drug associated side effects under monotherapy which hamper the delivery of treatment at effective doses.

PP-25

Gender differences: does it affect clinical characteristic and survival outcomes in adult acute lymphoblastic leukemia?

R. Cıftcıler[1], M. Levent[2], S. Aksu[1], N. Sayınalp[1], Y. Buyukasık[1], I. Haznedaroglu[1]
[1]Hacettepe University, Faculty of Medicine, Department of Hematology;
[2]Hacettepe University, Faculty of Medicine, Department of Internal Medicine

Objective: Acute lymphoblastic leukemia (ALL) is a hematological malignancy arising from lymphoblasts. While it is a relatively frequent hematologic malignancy in children with a higher incidence in boys, the incidence is uncommon in adults. The prognosis is good in childhood ALL however is poor in the adult form of the disease. The pathogenesis of ALL is complex, which probably originates from the complicated interactions between endogenous exposures, hereditary susceptibility and chance. The complexity of ALL has also been reflected in the various clinical characteristics of the two genders,

which demonstrates a regional and ethnic variance. We aimed in present study to compare the clinical characteristics and survival outcomes of ALL in adult male and female patients.

Aim: We aimed in present study to compare the clinical characteristics and survival outcomes of ALL in adult male and female patients.

Methodology: This study has been performed in a retrospective manner. Demographic and clinical data of the patients were obtained from hospital database. One hundred and one ALL patients who were diagnosed and treated in our tertiary care center between the years of 2003 and 2018 were evaluated.

Results: One hundred and one adult patients with ALL were included in this study. Sixty-one (60.4%) of patients were male and 40 (39.6%) patients were female. Median follow-up duration for all patients was 20.5 months (range, 0.5-161 months). The majority of cases were B-cell in origin in females, 39 patients (97.5%) were B-ALL and 1 (2.5%) of the patients were T-ALL. There were 46 patients (75.4%) with B-ALL and 15 (24.6%) patients with T-ALL in male patients. The incidence of T ALL was significantly higher in male patients than in female patients (p=0.003). Philadelphia chromosome (Ph+) positivity was determined in 3 (7.5%) patients in females and 2 patients (3.3%) in males (p=0.33). The median age was 34 (18-63) for females and 27 (17-79) for males (p=0.44). After induction chemotherapy, 29 patients (72.5%) achieved complete remission in females and 45 patients (73.8%) achieved complete remission in males (p=0.88). After induction chemotherapy, 9 (22.5%) patients died in females and 10 (16.4%) died in males (p=0.54). Five-year OS were 57% in males and 39% in females (p=0.14). Five-year DFS were 68% in males and 37% in females (p=0.02).

Conclusion: In conclusion, ALL incidence was higher in men than women among adult patients. However, there was no evidence of a gender difference in OS. DFS was statistically significant higher in males than females. Median age of the patients at diagnosis, detection of Ph+, achieved complete remission after induction chemotherapy and OS were similar between males and females. DFS was statistically significant higher in males. Additionally, a significantly higher proportion of T-cell ALL was identified in male patients. Whether significant gender differences reflected in the present study needs more clinical data to certify.

PP-26

Short-term survival outcomes and clinical characteristic of adult acute myeloid leukemia patients

R. Ciftciler[1], M. Levent[2], I. Haznedaroglu[1], O. Ozcebe[1], S. Aksu[1]
[1]Hacettepe University, Faculty of Medicine, Department of Hematology;
[2]Hacettepe University, Faculty of Medicine, Department of Internal Medicine

Objective: Acute myeloid leukemia (AML) is the most common acute leukemia in adults. More than 80% of patients with AML are provided with complete remission (CR) by widely used induction chemotherapy. However, because of early relapse, failure of induction chemotherapy and due to therapy-related mortality, the rate of long-term disease-free survival (DFS) in adults diagnosed with AML is poor. Several factors have been associated with worse outcomes, including unfavorable cytogenetics at diagnosis, duration of first CR less than 12 months, older age, and prior history of hematopoietic stem cell transplantation (HSCT). We aimed in present study to represent the clinical characteristics and short-term survival outcomes of adult AML patients.

Aim: We aimed in present study to represent the clinical characteristics and short-term survival outcomes of adult AML patients.

Methodology: This study has been performed in a retrospective manner. Demographic and clinical data of the patients were obtained from hospital database. Sixty-eight AML patients who were diagnosed and treated in our tertiary care center between the years of 2015 and 2018 were evaluated.

Results: Sixty-eight adult patients with AML were included in this study. Thirty-six (52.9%) of patients were male and 32 (47.1%) patients were female. Median follow-up duration for all patients was 13.3 months (range, 0.7–43.1 months). Median age of the patients was 46.5 (19–74) years. Relapse was observed in 20 patients (29.4%) in the follow up. Non-relapse mortality was seen in 9 patients (13.2%). The number of patients classified with Eastern Cooperative Oncology Group performance status 0, 1, 2 and 3 were 1 (1.5%), 36 (52.9%), 20 (29.4%) and 11 (16.2%), respectively. Karyotype analyses were available for 56 patients: two patients (2.9%) were classified in the favorable-risk group, 31 patients (45.6%) were in the intermediate-risk group and 23 patients (33.8%) were in the adverse-risk group, according to the European Leukemia Net classification. Sixty-five patients received idarubicin and Ara-C as induction chemotherapy and 3 patients received mitoxantron and Ara-C chemotherapy. Forty-four patients (64.7%) underwent alloHSCT. In the follow up 23 patients (33.8%) died. Three patients (4.4%) died in the first 60 days after diagnosis. Sepsis was the cause of the death in the first 60 days after diagnosis. Three-year overall survival was 54% in all patients. Five-year survival could not be reached. Three-year event-free survival was 46% in all patients. Median time was 26.4 months (9.2–43.6) for event-free survival.

Conclusion: The outcome of patients with AML is heterogeneous. It is therefore imperative to identify patients at high-risk for relapse who may benefit from more intensive induction or post-remission therapy. The cytogenetic and molecular markers are the best predictors of survival in AML patients. Moreover, early flow MRD (minimal residual diseases) during aplasia after the induction chemotherapy can also predict DFS and might play a significant role in the planning of post-remission therapy for patients at a high risk. However, these tests cannot always be done. The individual selection of therapy requires a strong prognostic, quick, basic, and accurate indicator of the response in patients with AML.

PP-27

Epigenetic therapy in childhood acute myeloid leukemias

A. Popa[1], V. Nemirovchenko[1], O. Tiganova[2], N. Subbotina[1], I. Serebryakova[1], A. Palladina[1], N. Tupitsin[1], B. Kurdjukov[1], T. Valiev[1], G. Mentkwvich[1]
[1]Federal State Budgetary Institution, N. N. Blokhin National Medical Research Center of Oncology of the Ministry of Health of the Russian Federation (N. N. Blokhin NMRCO); [2]Morozovskaya Children's Hospital of Moscow Ministry of Health

Objective: The results of treatment children with acute myeloid leukemia (AML) are not satisfied yet. The standard chemotherapy allows achieving complete remission in 92–96% of patients, but cumulative incident of relapse (CIR) and event free survival (EFS) are not good yet. Certain cytogenetic abnormalities and gene mutations are well-known and have been recognized in the WHO classification. AML results from collaborating genetic aberrations in at least 2 different classes. Type I aberrations induce uncontrolled proliferation and/or survival of the leukemic cells and are often represented by activating mutations in genes involved in signal transduction pathways. Type II aberrations inhibit cell differentiation and mainly result from genetic aberrations in hematopoietic transcription factors. However, certain aberrations found in AML, including those related to epigenetic deregulation, do not completely fit into the current type I and type II classification. Research into the epigenetic control of gene expression in AML, including histone modifications, DNA methylation, promises better understanding of the biological nature of the disease. The study AML NII DOG 2012 was the first protocol with combination of chemotherapy and epigenetic therapy (ET).

Methodology: From 01.2013 to 09.2018 31 pts were enrolled in NII-DOG-AML-2012 study and 52 pts treated with AML BFM 2004. There was no any difference of age, sex, and risks of diseases between two groups. All pts with HR and IR received treatment by 5 courses (AIE, HAM, AI, hAM, HAE) and with SR – 4 courses (AIE, AI, hAM, HAE). Epigenetic therapy based on combination of Valproic acid (VA) during 78 weeks, All Trans Retinoic Acid (ATRA) 1–43 days and for 14 days with the every post induction chemotherapy course and Decitabine 20 mg/m[SUP2] for 5 days in "window" regime in 5 pts and 26 pts got it on days 16–20 from the beginning AIE.

Results: There were neither any toxicity, no decrease of blasts in BM and peripheral blood after Decitabine in "window", one of the 5 patients developed relapse and one died from severe infection, three pts are still alive, and two got haplo-HSCT. All the pts who got Decitabine on 16–20 days achieved CR after induction comparing to 82.6% who were treated with the same chemo only (p=0.04). 4-years CIR was 26% and EFS – 66.9±12.4% median follow up 42.5±4.4 mo compare to 54.2±8%, median follow up 41.7±4.3 mo (ns) and OS – 81.2±9.8% median follow up 46.7±7.9 mo vs 71.4±6.6%, median

follow up 54.4±4.2 mo (ns). None of the patients with ET got allo-HSCT, but 6 (12%) from 52 pts in group just with chemo got allo-HSCT.
Conclusion: Thus, epigenetic therapy increases CR count and survival of children with AML. The place of demetilating agent in AML therapy has to be used in aplasia period after the first course of induction on time with minimum blasts count. Probably it is possible to do additional 5-days course of Decitabine after HAM for pts with HR and IR or after AI for SR.

PP-28

The investigation of plasma viscosity and endothelial dysfunction markers between patients diagnosed with essential thrombocytosis and reactive thrombocytosis

D. Karıs[1], T. Ozkan Tekın[2], G. Cetın[3], A.M. Ercan[4]
[1]Istinye University, Medical Faculty, Department of Biophysics; [2]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Hematology Section; [3]Bezmialem University, Mediacl Faculty, Department of Internal Medicine, Hematology Section; [4]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Biophysics

Objective: Essential thrombocytosis (ET) is a rare stem cell disease causing increased platelet numbers with impaired function. Biomechanical force applied by plasma viscosity-a major determinant of blood flow-alterations on endothelium, induces endothelial cells for secretion of endothelial dysfunction markers. The aim of our study is to investigate the relationship between plasma viscosity and nitric oxide (NO), asymmetric dimethylarginine (ADMA), vascular cell adhesion molecule-1 (VCAM-1) and intracellular adhesion molecule-1 (ICAM-1) as endothelial dysfunction markers in plasma.
Methodology: The study groups were randomly classified as ET-Group (n=40), IDA-RT-Group (reactive thrombocytosis related with iron deficiency anemia) (n=40) and HC-Group (healthy controls) (n=40). Plasma viscosity was measured utilizing Harkness capillary viscosimeter. Plasma levels of endothelial dysfunction markers were analysed with enzymatic method. ANOVA, Kruskal-Wallis tests and Pearson correlation test were used for statistical analysis.
Results: Plasma viscosity and plasma VCAM-1 levels were statistically higher in ET and IDA-RT Groups than HC-Group ($p<0.01$ and $p<0.01$). Plasma ADMA level was higher in HC-Group compared with ET and IDA-RT Groups ($p<0.05$ and $p<0.05$). HC-Group had higher plasma ICAM-1 levels compared with ET-Group ($p<0.05$).
Conclusion: Our novel study is a pilot study investigating the relationship between plasma viscosity and endothelial dysfunction markers as ADMA, VCAM-1 and ICAM-1. No significant difference in plasma nitric oxide synthase (NOS) levels among study groups and decreased ADMA levels in thrombocytosis groups might indicate that endothelial dysfunction cannot be detected quantitatively by means of NO and ADMA. Plasma viscosity, fibrinogen and VCAM-1 increased concurrently in thrombocytosis groups that might be an indicator of endothelial inflammation. In conclusion, it can be estimated that endothelial dysfunction has started and endothelium has been transforming into a pro-thrombotic and pro-atherogenic surface. We hypothesize that plasma viscosity and endothelial dysfunction markers can be used routinely in diagnosis, treatment and follow-up of patients diagnosed with ET for the determination of alterations of blood flow and endothelial dysfunction.

PP-29

Adult-onset ligneous gingivitis associated with plasma cell dyscrasia in the absence of plasminogen deficiency

E. Aksoy, M. Güzel Mastanzade, S. Kalayoğlu-Beşışık
Istanbul University, Istanbul Medical Faculty, Department of Internal Medicine and Hematology

Background: Ligneous gingivitis is a rare progressive destructive membranous periodontal disease presenting as nodular gingival enlargement with ulceration. It was often reported as part of a systemic disease due to quantitative or functional plasminogen deficiency and related fibrin deposition. Plasminogen is involved in degradation of fibrin, wound healing, cell migration, tissue formation, and angiogenesis. An impairment in plasminogen activity triggers inflammation, which leads to the increasingly woody membranes.
Case report: Forty-year-old male patient presented with acute onset hemoptysis and chest pain without noteworthy family history. He was not a smoker and denied environmental exposure. Physical examination was unremarkable except for small, yellow–brown papular lesions on periorbital and genital region skin, lips and buccal mucosae, and ulcerated thickened tongue. He had mildly decreased hemoglobin level (12.9 g/day) with normal MCV. The screening tests of hemostasis were within normal limits. No biochemical abnormality suggesting inflammation or infection was documented. Chest radiograph and high-resolution CT were normal, without any mass or paranchymal lesion. For connective tissue disease associated lung disease serologic markers including ANA, anti dsDNA, ANCA, anti-GBM were proved to be negative, and pathergy test for Behçet's disease was also negative. Echo-cardiograpy excluded cardiac pathology contributing pulmonary venous pressure and lung edema. On the other hand, increase in myocardial echogenicity and granular appearance were in favor of plasma cell dyscrasia, especially primarly AL amyloidosis suspicion. Lip biopsy was performed which showed Congo red negative amorphous eosinophilic colloid accumulation, which was consistent with Ligneous gingivitis was diagnosed. As a sign of plasminogen activity deficiency, its other frequent signs were evaluated. Ophthalmologic examination did not reveal ligneous conjunctivitis. Although the serum plasminogen level was within normal limits (0.084 g/L; N: 0.06-0,25). Despite that fresh frozen plasma as a source of plasminogen in combination with topical cyclosporine were started. To evaluate plasma cell dycrasia, bone marrow examination was performed and it revealed lambda type monoclonal plasma cell infiltration with a plasma cell ratio of 50%. He had massive proteinuria and lambda type Bence-Jones proteinuria. PET-CT showed one lytic lesion of 2x1.5cm, localized on T6 vertebral corpus (SUVmax: 6.8). Anti-myeloma treatment decision was made. During that time mucosal lesions as sign of ligneous gingivitis showed significantly regression. Plasminogen deficiency related tracheobronchitis was suspected as the reason for hemoptysis.
Conclusion: Plasminogen deficiency has emerged as a well-recognized disorder in which reduced levels of plasminogen lead to the development of pseudo membranes on mucosal surfaces, with subsequent end-organ damage. With a variety of genetic mutations, two types of plasminogen deficiency have been described in the literature. Type I represents a quantitative deficiency and type II a qualitative deficiency. Acquired plasminogen defect is seen with increased fibrinolytic activity. For our patient the clinical picture is consistent with deficient plasminogen activity, which could be related with late onset genetic disorder or multiple myeloma related high thrombolytic activity.

PP-30

The epidemiological patterns and comparative assessment of treatment options in chronic myeloproliferative neoplasms

V. Musteata
Institute of Oncology, S. U. M. Ph. "N. Testemitanu"

Objective: The objective of the study was to evaluate the epidemiological patterns, the short- and long-term results of treatment options in chronic myeloproliferative neoplasms (CMPN) in Moldova.
Methodology: The study enrolled 247 patients (pts) with different phases of idiopathic myelofibrosis (IM), chronic myeloid leukemia (CML) and polycythemia vera (PV), who had been treated and followed up at the Institute of Oncology during 1995-2018. The following research methods were used: epidemiological, descriptive statistics, comparative, clinico-analytic, cohortative. The diagnosis was proved by the histopathologic, cytologic, cytogenetic and molecular examinations of the bone marrow and peripheral blood.
Results: In 2016, 2017 and 2018 the incidence of myeloproliferative leukemias (C92) was respectively 2.5, 2.6 and 2.2, other leukemias (C93 C95)–3.5, 2.4 and 2.4 newly diagnosed cases per 100,000 population. Of the whole investigation totality, there were 30 (12.1%) pts with IM, 125 (50.6%) pts with CML and 92 (37.3%) with PV. The complete remission was obtained under the treatment

with chemotherapy and phlebotomies in 92 (100%) PV pts. The remission lasted 4–9 months (median 6 months) in group of pts treated with busulfan. The remission ranged between 3–8 months (median 5 months) under the treatment with hydroxycarbamide. The overall 5-, 10- and 20-years survival was 97.4%, 86.9% and 46.8% respectively in the group of pts treated with busulfan. The overall 5-, 10- and 20-years survival was 100%, 85.2% and 47.9% respectively in the group of pts under the treatment with hydroxycarbamide. Two (2.2%) pts with the relapse of PV underwent the immunotherapy with interferon-alpha and achieved a long-lasting remission of 61 and 79 months. Another 2 (2.2%) PV subjects with relapsed/refractory thrombocytosis were successfully treated with anagrelide. The remission rate and overall survival proved to be lower under the single-agent chemotherapy in IM pts than in those with PV. The complete hematologic response was obtained in 85.1% of CML cases under the therapy with tyrosine kinase inhibitors (TKIs) via MAS program, and yielded to be much higher ($p<0.05$) than the complete response rate registered after non-TKIs chemotherapy and interferon-alpha (27.5% of cases). The complete molecular response was achieved in 26.3% of cases with TKIs treatment. The 3-year relapse-free survival proved to be superior ($p<0.05$) in patients treated with TKIs (78.5%), than in pts under the non-TKIs therapy (17.4%). The overall 1- and 5-year survival was 97% and 64% respectively in the group of pts treated with TKIs and yielded to be superior ($p<0.05$) to that obtained under the non-TKIs chemotherapy (36.5%). Being well monitored, MAS program ensures an efficient management of this severe myeloproliferative malignancy. The overall survival of IM pts proved to be intermediate to that of pts with PV and CML.

Conclusion: CML yielded to be most frequent CMPN. There was no significant difference between the long-term results of treatment with busulfan and hydroxycarbamide in combination with phlebotomies in PV. The enrollment of CML patients in MAS program and the administration of TKIs significantly favored the short- and long-term results of treatment, committing to the improvement of the performance status and resumption of the daily activities.

PP-31

Autoimmunity associated with hepatitis C virus

A. Amına, G. Sabıha, M. Hacene
Badji Mokhtar University Medicine Faculty, University Hospital Center, Annaba, Algeria

Objective: HCV is a hepatotropic virus, but also lymphotropic. This lymphotropism is responsible for the activation and proliferation of B lymphocytes, with the main consequence being the production of autoantibodies (auto-Ab). The overall prevalence of these is very variable: 15 to 65%, and depends on the population studied (ethnic origin) and the positivity threshold used for the detection of auto-Ab. The association between autoimmunity and viral hepatitis C is not without posing many problems to the practitioner; this becomes more difficult when it comes to a combination of chronic viral hepatitis C and autoimmune hepatitis (HAI). This work aims to report the auto-Ab profiles of 82 patients with HCV.

Methodology: The study involved 82 sera from HCV patients (49 men and 33 women with a mean age of 50±16 years). Of these patients, 59.79% had post viral hepatitis C chronic and 40.24% were referred for pre-treatment assessment. The assessment concerned the search for non-organ specific anti-tissue antibodies found during autoimmune liver diseases and the search for anti-nuclear antibodies (ANA).

Results: The search for non-organ specific anti-tissue antibodies was positive for 65.85% of which: 50% are anti-smooth muscle antibodies, 17.07% are smooth muscle antibodies (anti-Factin) and 1.22% are anti-parietal cell antibodies. 34.15% of the sera are negative in ANSO. For ANA testing, it was positive for 40.24% of the sera and showed a heterogeneity of autoantibodies as follows: 29.27% were speckled, 4.88% homogeneous, 3,6% nucleolar, 2.44% centromere and 1.22% nuclear dot multiple and 1.22% membrane aspect. 59, 76% of the sera are negative in ANA.

Conclusion: The significance of these auto-Ab is not clear: non-specific consequence of a liver disease (especially as the disease is advanced); control of an auto-immune fiel constituting a co-factor of aggravation of the liver disease; or auto-Ab induced by viral infection.

PP-32

Morbidity symptoms of myeloproliferative neoplasia

M. Altareb, B. Alharbi, A. Alahmari, H. Alzahrani
King Faisal Specialest Hospital and Research Centre

Objective: Myeloproliferative neoplasia (MPN) is a group of diseases in which myeloid cells proliferate in mature and immature manners. It consists of 3 disorders that's include Essential thrombocythemia (ET), polycythemia vera (PV), and Myelofibrosis (MF). The combined annual incidence rate for PV, ET, and MF were 0.84, 1.03, and 0.47 per 100,000 respectively 2. The Myeloproliferative neoplasia (MPN) has comorbid symptoms that are affecting patient's quality of life and daily activity. The severity ranging from patient to patient depending on type, stage of disease and whether the patient receiving therapy or not. Our objective of this abstract is to determine the severity of MPN symptoms and correlation to MPN subtypes.

Methodology: The study design is a descriptive retrospective analysis of MPN registry patients in single-center done at King Faisal specialist Hospital and Research center. From our MPN registry, we able to assess a total of 132 patients, 68 males, 64 females. 70, 46 and 16 of Essential thrombocytopenia (ET), polycythemia vera (PV) and myelofibrosis (MF), respectively. By using myeloproliferative neoplasia symptoms assessment form (MPN-SAF) Which has 10 symptoms these are: fatigability, early satiety, abdominal discomfort, inactivity, concentration problems, night sweating, itching, bone pain, fever and unintentional weight loss. Each symptom graded from 0–10, in which 0 means not complain of the symptom, and 10 is maximus severity of symptom. We used direct phone contact to each patient asking them these questions and we filled up the questioner per their answers.

Results: Inactivity has the most comorbid symptoms in all MPN 63.6% followed by fatigability 59.8%, abdominal discomfort 53.8%, night sweat 43.9%, bone pain 40.9%, itching 38.6%, concentration problems 35.6%, early satiety 31.1%, weight loss 22.7%, fever 5.3% respectively. Because of the inactivity is the most prevalence, majority of PV patients 65.2% suffering from it, followed by 64.3% in ET, 56.2% in MF. The maximum MPN SAF score recorded is 92 in ET, 74 in PV, and 61 in MF. 65.9% of these patients on cytoreductive therapy were 34.1% not. We found that the percentage of all group who are on cytoreductive medications are similar. 67.1% of ET patients on cytoreductive agents, 65.2% of PV, and 62.5% of MF.

Conclusion: Significant number of MPN patient suffering from the comorbidity of the disease. More than 63% complain from fatigability as major symptoms despite that most of them taking cytoreductive therapy. The mean MPN-SAF score was significant in MF 29, followed by ET 18.5, PV 16.5.

PP-33

Modern approaches to diagnosis and treatment of various clinical forms of polycythemia vera

F. Khalilova, A. Kerimov, A. Hasanova
Scientific Research Institute of Hematology and Transfusiology

Background: In recent years clarified that hemoglobin and a hematocrit levels of polycythemia vera (PV) patients can be below the diagnostic criteria of WHO 2008. Hypodiagnosis of PV can lead to decrease in intensity of therapy and worsen efficiency of treatment. Implementation of new diagnostic criteria of PV (WHO of 2016) promotes more accurate definition of clinical forms of a disease and particularly the latent (masked) form of PV.

Case report: The patient, A.I.,1975 date of birth, female, in 12.10.2015 was examined in the city Barda because of the thrombophlebitis of the lower extremities. Due to the changes in a hemogram she was sent for consultation to the hematologist. In 02.11.15 the patient was examined in Scientific Research Institute of Hematology and Transfusiology. Complaints during receipt were connected with a plethora (an aquagenic itch, a hyperemia of the face, etc.) and a varicose of the right lower extremity (edema in leg, feeling of pain, etc.). The spleen was palpable from under a costal arch for 5 cm. In a hemogram: Hb 150 q/l, RBC 4.8×10^{12}/l, PLT 624×10^{9}/l, WBC 15.4×10^{9}/l, Ht 53.6%. Histological examination of the bone marrow revealed the expansion of all three hematopoietic cell lines. As a result of the molecular and genetic analysis (PCR method) a mutation of JAK2V617F (34.499) was found. A

patient was diagnosed with polycythemia vera. Because of boundary level of hemoglobin, the phlebotomy (FT) was not used as first line therapy. In the course of treatment in steps and depending on the response to treatment the cytostatic-Hydrea, antiaggregants and H2 blockers of histamine receptors were used. Due to the bad tolerance of the Hydrea an administration of this drug was cancelled and treatment continued with an antiaggregant. At the end of the 2016-th year a menometrorrhagia was observed in patient because of the left ovarian cyst. Antiaggregant was cancelled. The patient was several months on treatment and under attendance of the gynecologist. Cases of a menometrorrhagia were suspended, however in connection with the previous bleedings the iron deficiency anemia developed in patient, and the itch even more amplified. An iron therapy and an interferon therapy was appointed. Now the patient feels well. The painful aquagenic itch is not observed.

Methodology: We studied 193 PV patients during the years of 2014–2018. Data are obtained from our institute's databases. Diagnostic methods, a clinical manifestations and treatment methods of patients of PV were analysed. The WHO 2016 classification and the ELN recommendation was used.

Results: Out of 193 patients, 104 were male and 89 were female (1,16:1), median age was 56 (27–87 years). Histological examination of the bone marrow in patients with PV revealed the expansion of all three hematopoietic cell lines. Reticulin fibrosis (MF-1) was determined in 2.9% of patients, MF-2 in 5.7% of patients, in other cases there were no signs of fibrosis (MF-0). The JAK2V617F mutation was detected in 97% of patients; in exon 12 JAK2 mutation was not detected. Average allelic load in JAK2V617F was 41% (3–90%). Cytogenetic studies were performed in 66 patients, abnormalities were detected in 13.7% of patients (del (20q); +8; +9; absence of Y chromosome). The number of patients with thrombotic complications was 22 (11.4%), arterial thrombosis was observed more often than venous. In 6 patients reccurent thrombosis were noted. Out of 193 PV patients, 66 (34.2%) patients were diagnosed with latent form PV and 127 (65.8%) patients with classic form PV. In five years 9 patients (4.7%) transformed to myelofibrosis, 4 patients (2.1%) had a blast transformation of the disease. The latent form of a disease was observed mainly in younger patients. They had lower levels of HGB, RBC, HCT, JAK2V617F allelic load, higher levels of PLT and more often thrombotic complications. Patients received the following types of therapy: a phlebotomy-aspirin – 30 patients (23%), a hydroxycarbamide – 94 (49%),an interferon alfa-2 beta – 27 (14%), a phlebotomy-interferon 7 (3%), a flebotomy -hydroxycarbamide – 21 (10.8%), other – 14 (7.2%). The response to therapy was evaluated according to criteria of ELN 2014. The complete clinical and hematological response was at 52 (26.9%) patients, the partial clinical and hematological response at 121 (62.6%) patients, 20 patients (10.4%) had no response to treatment.

Conclusion: The analysis of PV patients according to the new diagnostic criteria of WHO 2016 allowed to review the diagnosis of PV and to identify latent PV at 1/3 of patients. The most informative way of diagnosis of the latent form of PV is trephine-biopsy of bone marrow. On time diagnosis of the latent form is important for optimization of treatment of PV. However, in general PV has favorable prognosis, decrease in intensity of therapy can lead to increase in frequency of thromboses.

PP-34

Association of human leukocyte antigen groups with oral mucositis in patients undergoing bone marrow transplantation

A. Tufan[1], F. Oguz[2], F. Tufan[1], C. Kekık[3], F. Bılgın Tarakcı[4], D. Sargın[5], S. Kalayoglu Besısık[5]

[1]Istanbul University Istanbul School of Medicine Department of Internal Medicine; [2]Istanbul University Istanbul School of Medicine Department of Medical Biology; [3]Istanbul University Istanbul School of Medicine Department of Medical Biology; [4]Istanbul University Istanbul School of Medicine Department of Internal Medicine; [5]Istanbul University Istanbul School of Medicine Department of Hematology

Objective: Oral mucositis (OM) after hematopoetic stem cell transplantation (HSCT) may lead to toxicity which impairs quality of life. Associations between several diseases and human leukocyte antigen (HLA) groups have been long recognized. A genetic contribution as the association of HLA groups with OM after HSCT, has not been reported to date. We aimed to assess whether an association of HLA phenotype and presence and severity of OM after allogeneic HSCT exists.

Methodology: This prospective and observational study was conducted in patients who underwent HSCT. OM was assessed by documenting its severity according to WHO scale with clinical questioning and examination. All patients and donors were already HLA typed. All patients received the same oral health care with nystatin and chlorhexidine rinse and vitamin E application when mucositis developed. The association of OM duration and maximum severity with gender, age, HLA alleles, diagnosis, conditioning regimen, stem cell source, engraftment times, and complications were investigated.

Results: A total of 45 patients were enrolled. All the patients with HLA B44 type developed mild OM while all patients with HLA DR15 type developed severe OM. HLA A23, HLA B21, HLA B44, HLA DR15, and HLA DR11 were associated with shorter OM duration while HLA A26 and HLA B52 were associated with longer OM duration. Myeloablative conditioning regimen and longer duration of neutropenia were associated with longer OM duration. Regression analysis revealed that HLA B44 and HLA-DR11 as independent factors associated with OM of milder severity and shorter duration. Neutrophil engraftment time was independently associated with longer duration of OM but not with OM severity. None of the other factors were independently associated with OM of greater severity or longer duration.

Conclusion: There are some studies documenting association between certain HLA types and inflammatory diseases where cytokines may play a key role. OM has multifactorial ethiopathogenesis and cytokines are thought to play an important role. We identified that some HLA alleles were associated with OM severity and duration. These findings may facilitate predicting risk of morbidity and may provide incorporation of individualized preventive and treatment approaches provided that these results are validated in larger prospective studies.

PP-35

The efficacy of reuse therapeutic plasma exchange in relapsed/refractory immune-mediated thrombotic thrombocytopenic purpura: a single-center experience of 130 cases

M. Güzel Mastanzade, S. Kalayoğlu Beşışık, S. Altay Dadın, M. Aktan, İ. Yönal Hindilerden, M. Yenerel, M. Nalçacı

Istanbul University, Faculty of Medicine, Department of Internal Medicine, Division of Hematology

Objective: Immune-mediated thrombotic thrombocytopenic purpura (iTTP) results from severe acquired ADAMTS13 deficiency due to inhibitory auto-antibodies. ADAMTS13 is the enzyme, responsible for cleaving large von Willebrand factor (vWF) multimers into smaller, less thrombogenic units. In iTTP, the resultant accumulation of ultralarge vWF multimers leads to uncontrolled platelet thrombus formation in the microvasculature when untreated, can result in end-organ damage, cardiovascular collapse, and death. Treatment with steroid as immunsupressive and therapeutic plasma exchange (TPE) to restore ADAMTS13 activity by replacing the enzyme and removing autoantibodies has lowered the mortality rate of to less than 10%. Relapse remains the central concern for iTTP survivors Aim: We investigated retrospectively iTTP patients focusing on the relapse rate and possible influencing factors including management types.

Methodology: The medical records of all relapsed/refractory iTTP patients treated between February 2006 and July 2019 were reviewed. Patient's demographics, laboratory findings, relapse data and outcomes were recorded.

Results: The study included 130 iTTP patients (female/male; n=99/31) and 436 (3–51) TPE sessions. Relapse was observed in 17 patients (13%) (median age: 32.1±4.94 years (range 19–56). The relapse number per patients was 2.9±2.5 (2–12). Women suffer significantly more frequent relapses (14 women and 3 men). At relapse all patients underwent TPE, 4 patients did receive rituximab and 6 patients underwent splenectomy in addition to TPE whereas 2 splenectomized patients had received also rituximab. Splenectomy and rituximab usage did not change the number of TPE at subsequent relapses (p=0.224 and p=0.09). Relapses were with less severe clinical signs

compared with initial presentation. TPE session number to achieve remission was proved to be lower at relapse (mean n=6.5±4.8) compared to at first presentation (mean n=13.4±13.9) (p=0.014). In three patients one of relapses occurred during pregnancy. Interestingly, one patient's relapse was with Hodgkin's lymphoma after 5 years of the first presentation. Two patients (11%) died during follow-up. Infection and bleeding were the causes of death, respectively.

Conclusion: It is well established that most iTTP suffer relapse after initial response without clear predictors. Pregnancy, infection, vaccination, drugs and/or each relapse may be the clinical risk factors for subsequent relapses. In our study, all relapses were clinically overt and some of them had predictive factors. There is not any standard management for relapsed iTTP but experiences shows that relapses were with lesser severity and achieve more rapid response. Thus, documentation of impending relapse such as by laboratory analyses would carry forward preemptive treatment and may reduce relapse rate from inevitable fate of iTTP.

PP-36

Serological weak d phenotypes and RHD genotype frequency among Turkish blood donors

M. Yanaşık[1], S. Kalayoğlu Beşışık[1], G. Öztürk[2], M. Huslu[1], S. Temurhan[1], S. Akgül Usta[1], H. Şentürk Çiftçi[1], F. Aydın[3], F. Savran Oğuz[1]
[1]Istanbul Medical Faculty Blood Center, Istanbul University, Istanbul, Turkey; [2]Department of Pediatric Hematology/Oncology & Bone Marrow Transplantation Unit, School of Medicine, Altunizade Hospital, Acıbadem University, Istanbul, Turkey; [3]Istanbul Science University, Department of Medical Biology, Istanbul, Turkey

Objective: The Rh blood group system is one of the most polymorphic and immunogenic systems. All Rh antigens are controlled by 2 linked genes; RHD and RHCE gene. D typing based on detection of the entire protein D antigen the most immunogenic antigen on red cell membrane. RHD gene polymorphisms causes differences in D antigen expression, namely, molecularly defined weak D phenotypes, partial D phenotypes and DEL phenotypes which play important role in transfusion practice. AIM: Variant D genotypes distribution was assessed.

Methodology: RhD blood group phenotyping were performed by gel centrifugation/column agglutination method with polyclonal anti-D blood group reagents. Donors' samples giving no or weak (<+4) reactivity in initial testing were tested by indirect globulin tests (IAT) with potent anti-D reagents. All IAT positive samples were tested also by direct antiglobulin (DAT) test. All DAT positive samples were excluded from the study. The remaining donors' with IAT-positive and DAT-negative samples have been accepted as weak D and were called back for PCR-genotyping. RHD genotyping was performed by using ready-to-use PCR-SSP commercial kits BAGene Partial D-TYPE kit and BAGene Weak D-TYPE kit (BAG Health Care GmBH, Lich, Germany).

Results: Between January 2011 and February 2017, 177.554 donors were assessed. By routine analyses RhD negative phenotype frequency was found to be 15.11% (n=26.822) whereas 228 (0.12%) of them had been defined as having weak D phenotype. 67 of donors turned back to recall. Among genotyping, 68.7% had weak D and 22.4% partial D. Six cases (8.9%) were not identifiable. Among weak D genotype, type15 (26.9%), type 11 (14.9%) and type 1 (13.4%) were the most frequent genotypes.

Conclusion: The prevalence of serological weak D phenotypes varies by race and ethnicity. An estimated 0.2–1.0% of Caucasians inherit an RHD genotype that codes for a serological weak D phenotype. Our serologic weak D phenotyping showed a few lesser frequencies. Most serological weak D phenotypes in Caucasians express molecularly defined weak D types 1, 2 or 3 whereas our finding indicates the most frequent genotypes as in order type 15, 11 and 1. For transfusion practice a weak D test is required if a blood donor's typed as D negative. Blood donors with a serological weak D phenotype should be managed as RhD-positive, in contrast to transfusion recipients and pregnant women, who should be managed as RhD-negative. We think that clinical laboratories should implement policies to increase detection of serological weak D phenotypes and resolve their interpretation by RHD genotyping, not avoid their detection or make detection optional. In standard practice weak D typing may document types with increasing risk of alloanti-D forming types. The present work was supported by the Research Fund of Istanbul University. Project No. 40636

PP-37

A rare complication of hematopoietic stem cell transplantation: Kaposi sarcoma

H. Bekoz, A. Sağırlı, O. Türk, B. Ceylan, D. Sargın
Medipol University

Background: Kaposi sarcoma is a neoplasm characterized by mucocutaneous and visceral angioproliferations that requires infection with human herpes virus (HHV)-8 for its development. The iatrogenic variant is seen in patients undergoing immunosuppressive therapy, especially in organ transplant recipients. Kaposi sarcoma after hematopoietic stem cell transplantation is a rare complication with only 18 cases reported previously.

Case report: Here we present the case of a 58-year-old male patient treated for acute B lymphoblastic leukemia. For his second relapse, he was started on hyper-CVAD regimen after which he underwent an allogeneic stem cell transplant from human leukocyte antigen-identical unrelated donor. Prompt donor engraftment was achieved. The only immunosuppressive he received was cyclosporin A, which was stopped 90 days after the transplantation. He received multiple blood transfusions because of his ongoing anemia. He was diagnosed with direct Coombs positive hemolytic anemia caused by subgroup mismatch (anti-E and anti-Jka) on day +219. He was started on prednisone. He developed small purple papillary lesions on his right leg and penis on day +255 while receiving steroid therapy. This coincided with the high levels of cytomegalovirus DNA in his whole blood, which was also positive for HHV-8 DNA when analyzed with PCR. A punch biopsy of the lesion was obtained which was reported to be Kaposi sarcoma with positive immunohistochemical staining for HHV-8. Both the recipient and the donor were seronegative for HIV before the transplant; recipient remained seronegative. CT of the chest and abdomen excluded visceral involvement. Ultrasonography revealed an enlarged lymph node that was confirmed to be Kaposi sarcoma via core biopsy. Since there were no visceral involvement, we only considered local therapies. Immunosuppressive therapy was reduced but could not be stopped because of his autoimmune hemolytic anemia. Radiation therapy was administered, one course for the lesion on the right leg and another for the inguinal lymph node. Lesions treated with radiation regressed, however non-irradiated lesions continued to progress, eventually involving his trunk, left leg, and face; each less than 1cm in diameter. Cryotherapy and topical 5-Fluorouracil were utilized for the skin lesions. Lesions regressed but never fully healed. He presented to the emergency department on day +387 with fever and productive cough. His sputum cultures produced Klebsiella pneumonia, so he was admitted and started on antibacterial treatment. During his stay, he developed CMV viremia. While under treatment he underwent septic shock and admitted to the intensive care unit. The patient died of cardiopulmonary arrest during his stay in the intensive care unit. The major risk factors for our patient were the immunosuppressive therapy and concurrent cytomegalovirus infection. Multiple blood transfusions he received might have been responsible for a primary infection with HHV-8.

Conclusion: In conclusion, Kaposi sarcoma is a rare complication of hematopoietic stem cell transplantation that should be thought of in any immunocompromised patient with unusual mucocutaneous lesions.

PP-38

Results of escBEACOPP therapy in children with Hodgkin's lymphoma (II+bulky, III, IV studies)

E. Belyaeva, N. Kulichkina, N. Batmanova, A. Popa
Blokhin's National Medical Research oncology center

Objective: The treatment results of children with advanced stage (II+bulky, III, IV studies) of Hodgkin's lymphoma are not satisfied. We decided to study efficacy and toxicity of chemo (escBEACOPP).

Methodology: From 2003 to 2019 126 pts (female 61, male 65) with advanced stage Hodgkin's lymphoma were enrolled in this study. The median age

was 12.5 years (3–18). Primary staging was: stage II – 41 pts (32.5%) with bulk disease (mediastinal mass greater than 1/3 of the mediastinal thoracic diameter and/or nodal aggregate greater than 10 cm), stage III – 26 pts (20.6%), stage IV – 59 pts (46.9%). Therapy induction consisted on 4 courses of escBEACOPP (cyclophosphamide 1200 mg/m^2/day, day 1; etoposide 200 mg/m^2/day, days 1–3; doxorubicin 35 mg/m^2/day, on day 1; bleomycin 10 U/m^2/day, day 8; vincristine 1.5 mg/m^2/day, day 8; procarbasine 100 mg/m^2/day, days 1–7; prednizone 20 mg/m^2/day, days 1–14). Consolidation was different for females and males and also depended on response to 4 courses of induction. Females with a good response to therapy (CR, PR1 - 70% reduction in disease) received 4 courses COPP/ABV (cyclophosphamide 600 mg/m^2/day, day 1; doxorubicin 35 mg/m^2/day, on day 8; bleomycin 10 U/m^2/day, day 8; vincristine 1.5 mg/m^2/day, day 1; vinblastine 6 mg/m^2/day, day 8; procarbasine 100 mg/m^2/day, days 1–7; prednizone 20 mg/m^2/day, days 1–14) without RT. Male with CR or PR1 received 2 courses ABVB (doxorubicin 25 mg/m^2/day, on days 1, 15, vinblastine 6 mg/m^2/day, days 1, 15, bleomycin 10 U/m^2/day, days 1, 15, dacarbazine 375 mg/m^2/day, days 1, 15) with involved field RT 20 Gy. All slow responders pts (PR2 - <70% reduction in disease) received 4 additional courses of escBEACOPP followed by RT.

Results: Complete response after 4 courses got 39 pts (31%), PR1 – 70 pts (55.5%), PR2 – 16 pts (12.7%), SD – 1 pts. Forty-eight females have not got RT(5 – developed relapse with a still but in second CR). Median follow-up is 174.2±2.3 mo, RFS 92.4±2.4%; EFS 90.9±2.6%; OS 97.6±1.4%. In spite of severe hematological toxicities – grade IV 45.6% just two patients had fatal infection and one grade III mucositis. There were no any non-hematological toxicity.

Conclusion: We suggest that aggressive therapy based escBEACOPP regimen is tolerable and shows good treatment results in patients with advanced stages HL.

PP-39

Idiopathic pulmonary hemosiderosis: a rare cause of chronic anemia

A. Butt, R. Ahmed, N. Iqbal, J. Khan, A. Rahman
Aga Khan University Hospital

Background: Idiopathic pulmonary hemosiderosis (IPH) is a rare disease marked by alveolar bleeding and subsequent accumulation of hemosiderin in the lungs. It classically presents as a triad of hemoptysis, iron deficiency anemia and alveolar infiltrates. The condition is more commonly found in children with an approximate incidence of 0.24–1.23 cases per million in different populations. 80% cases of IPH occur in children.

Case report: Here we present three cases of IPH: one pediatric and two adult cases. Both adults presented with hemoptysis, dyspnea and recurrent anemia while the pediatric patient presented with long standing anemia and dyspnea.

The first case is of a 26-year-old male who had previously received 5 packs of blood transfusion for low Hemoglobin of 5g/dl. Bronchoscopy confirmed alveolar hemorrhage. A diagnosis of IPH was made and the patient was treated successfully with prednisolone, azathioprine and ferrous sulfate.

The second case is of a 26-year-old female with a hemoglobin at presentation of 8.0g/dl, despite receiving blood transfusions previously. Her chest X-ray and CT scan findings were suggestive of interstitial lung disease. Lung biopsy findings were consistent with IPH. This patient was started on steroids but she did not respond. She died a few weeks later with respiratory failure secondary to hospital acquired pneumonia.

The third case is of a 7-year-old male with long standing anemia since the age of 2 years, despite receiving blood transfusions. He had a hemoglobin level of 3.2 g/dl at presentation. Upon subsequent admission, CT scan depicted evidence of diffuse ground-glass haze in bilateral lung fields, which led to suspicion of IPH and a subsequent lung biopsy confirmed the diagnosis. The patient was managed on oral corticosteroids and had multiple hospital admissions for pneumonia due to IPH. Later, the patient developed posterior reversible encephalopathy syndrome (PRES), possibly due to hypertension which was managed at our centre and the patient was discharged on amlodipine, atenolol, azathioprine, prednisolone and valproate sodium.

Conclusion: Given the severity of the illness, it is imperative for clinicians to consider IPH as an important differential in adult patients who present with diffuse alveolar hemorrhage and also in children with long standing anemia who do not respond to iron therapy. However other causes of alveolar bleeding must be ruled out before diagnosing a patient with this disease. This must be followed by a lung biopsy if possible to confirm diagnosis. There needs to be a greater awareness amongst physicians regarding IPH so that it can be correctly diagnosed and thus successfully treated.

PP-40

Epidemiology and clinical characteristics of acute myeloid leukemia: a retrospective analysis in Annaba, Algeria

F. Grıfı, S. Bougherıra, N. Djelamda
CHU Annaba Department of Hematology, Annaba, Algeria

Objective: Acute myeloid leukemia (AML) is the most common leukemia in adults. In Algeria, the incidence of acute myeloid leukemia (AML) was estimated to be 0.91 cases per 100,000 person-years, with a median age of 45 years in 2010.

Methodology: In this retrospective study, we report the incidence and the outcomes of patients with acute myeloid leukemia in Annaba, a major Algerian eastern city. We analyzed the records of all AML patients treated at the Department of Hematology of the university hospital of Annaba in Algeria, between January 1, 2013 and December 31, 2017.

Results: A total of 180 AML patients at diagnosis were identified. The calculated incidence rate was 1.2 cases per 100,000 person-years with a median age of 52 (range, 15–85) and 69% were male with a male to female (M/F) ratio of 1:16. At diagnosis, median white cell count was 50.7 (0.4–353)×10^9/L, hemoglobin 7.7 (4.4–15.8) g/dL, platelets 89 (6–650)×10^9/L, peripheral blasts 58% (0–100), and bone marrow blasts 62% (11–100). Regarding the French-American-British subgroups, M2 was the predominant subtype (39.8%) followed by M1 (19.5%), M4 (8.5%), M3 (3.9%), M5 (3.9%), M6 (1.5%), while 10,9% of cases were difficult to classify. Karyotype analysis was performed in 21% of patients, Recurrent chromosomal translocations such as t(8;21) is frequently detected (11,1%). Patients with complex karyotype (CK) had worse overall survival than those with fewer abnormalities or normal karyotype in all age groups. The frequencies of unsuccessful cytogenetics were 14.8%. The frontline induction chemotherapy with cytarabine + daunorubicin (7+3 regimen), was the most commonly used (69.5%), it showed the highest frequency of complete remission (CR) (90.7%). Overall Response Rate (ORR) was 46%. 10 HSCT were performed for AML (8 in first complete remission and 2 in second remission). Median Overall Survival (OS) was 7.5 (1–19) months. 38 patients (29.6%) died of complications during treatment, mainly infections.

Conclusion: In this study, we found out that there was a statistically significant increase in AML patients over the last five years in Annaba (13 cases in 2013, 52 in 2017), with high mortality rate and low 1-year OS, due to health care resource constraints and infrastructure and the significant barriers for access to HCT. Addressing these challenges will be required to improve the treatment and supportive care for patients with AML in our hematology department.

PP-41

The association between hemogram parameters and survival in advanced stage diffuse large B cell lymphomas

A. Yasın, N. Kyıo
Bezmialem University, Faculty of Medicine, Internal Medicine Department

Objective: The aim of this study was to evaluate hemogram parameters before and after treatment in patients with advanced stage diffuse large B cell lymphoma (DLBCL) and to determine the association between hemogram parameters and survival in DLBCL patients.

Methodology: The inclusion criteria were a histopathological and clinical diagnosis of de novo DLBCL grade 3 and 4 regarding Ann-Arbor staging system, high risk score of age adjusted international prognostic index (IPI), high ECOG performance status (3-4), treated with R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone) for at least 4 cycles and who had complete clinical data and follow-up from 2013 to 2019. We excluded patients with concomitant malignancy, chronic

inflammatory disease and/or regular antiaggregant, anticoagulant, anti-inflammatory drug use and who were lost to follow-up. 25 DLBCL patients (13 females/12 males) were qualified for the study. Hemogram, biochemistry parameters and maximum SUV max values in Positron Emission Tomography (PET-CT) and overall survival (OS) and progression free survival (PFS) values of the patients were retrospectively collected.

Results: The mean age of the patients was 48.68±12.9 years. The mean OS was 37.96±5.74 months, the mean PFS was 34.4±5.70 months and the mean SUVmax was 19.66±9.51 months. Pre-treatment platelet distribution width (PDW) (16.6±3.77 fl) was significantly lower than post-treatment PDW (18.26±3.67 fl) (p = 0.003). Pre-treatment neutrophil lymphocyte ratio (NLR) (7.88±2.09 fl) was significantly higher than post-treatment NLR (2.80±1.82 fl) (p=0.023). There was a positive correlation between pre-treatment LDH level and pre-treatment platelet level (r=0.50, p=0.01). While there was a negative correlation between MPV and PDW before treatment (r=–0.46, p=0.02), there was a strongly positive correlation with OS and PFS (r=0.83, p<0.001, r=0.79, p<0.001, respectively). While there was a strongly negative correlation between pre-treatment PDW and OS and PFS (r=–0.79, p<0.001, r=–0.81, p<0.001, respectively), there was a negative correlation between post-treatment PDW and OS and PFS (r=–0.53, p=0.01; r=–0.50, p=0.014, respectively).

Conclusion: In this study, we found that a high MPV and low PDW prior to chemotherapy was associated with increased OS and PFS in patients with DLBCL, which supports the findings of previous studies. Platelets are playing an important role in tumor-associated inflammatory response and cancer progression. Although the number of studies is limited, recent studies showed the negative effect of a low MPV on different types of lymphoma. More investigations with larger sample size are needed to explain the underlying mechanisms about the influence of platelets on the prognosis of DLBCL patients.

PP-42

Ibrutinib as a monotherapy for relapsed or refractory DLBCL patients: a single-center experience

O. Ekinci, M. Merter
Firat University, Faculty of Medicine, Department of Hematology

Objective: Ibrutinib is an oral covalent inhibitor of Bruton tyrosine kinase, which disrupts signaling from the B-cell receptor to NF-κB. Ibrutinib has shown activity in non–germinal center B-cell diffuse large B-cell lymphoma (DLBCL). In this study we aimed to evaluate the effectiveness of ibrutinib as a single agent in our relapsed or refractory DLBCL patients.

Methodology: We evaluate 6 patients who receive ibrutinib as a monotherapy for R/R DLBCL between May 2018 and June 2019. Patients' previous treatments, Ann-Arbor stages, comorbidities and responses to ibrutinib were identified.

Results: Six patients were evaluated. Median age was 71 (44–84). All patients were female. Five patients' Ann-Arbor stage were IV and one patient was stage III. Patients received median 3 (range 1–5) lines of therapy. Ibrutinib was administered to all patients as a single dose of 560 mg peroral daily. Three patients had no response to ibrutinib. Two patients had central nervous system (CNS) involvement at the time of relapse and both did not respond to ibrutinib. One patient had Richter transformation and she was the only patient that complete response was achieved. One patient had stable disease and one has partial response. As the moment 3 patients are still alive.

Conclusion: In a phase 1/2 clinical trial that involved 80 subjects with relapsed or refractory DLBCL, ibrutinib produced complete or partial responses in 37%. Our results were consistent with this study. Interestingly ibrutinib had no activity in our CNS involved patients despite its well-known CNS penetration. Another interesting finding of our study was that the only patient who achieved complete response had Richter transformation. All our patients had poor performance status and were not eligible for high dose therapies. Ibrutinib were well tolerated in all our patients and no adverse event was observed. Our study suggests that ibrutinib is a feasible choice for patients who are multi refractory and have poor performance status.

PP-43

Ruxolitinib for polycythemia vera and essential thrombocytosis: a single-center experience

O. Ekinci, M. Merter
Firat University, Faculty of Medicine, Department of Hematology

Objective: Ruxolitinib is a JAK1/2 inhibitor and was demonstrated to be effective in patients with primary myelofibrosis and in those with polycythemia vera (PV) who were resistant or intolerant to hydroxyurea. Ruxolitinib was also evaluated for essential thrombocytosis(ET) but no improvement was shown in treatment efficacy compared to best available therapy. Here we present our experience with ruxolitinib in PV and ET patients

Methodology: For this retrospective study patients who had a diagnosis of PV or ET and treated with ruxolitinib between March 2018 and June 2019 were evaluated. Patients who had progressed to myelofibrosis were excluded. Patients' hemogram parameters, spleen size, symptoms, previous treatments and adverse events were identified.

Results: Sixteen patients were evaluated. Median age was 73 (range 29–91). Eleven patients were female and 5 were male. Of the patients, 4 were PV and 12 were ET. Ten patients had bone marrow biopsy evaluation. There were grade 1 fibrosis in 9 patients and one patient had no fibrosis before ruxolitinib treatment. Five patients had splenomegaly. Median spleen long axis measurement was 12 (range 10–31) cm. Before ruxolitinib, 14 patients received hydroxyurea, 10 received anagrelid and 7 received classical interferon. Four patients were intolerant to previous therapies and 12 were resistant. Patients received ruxolitinib for median 9 (range 2–14) months with a median dose of 25 mg (range 10–40). Pneumonia was developed in 2 patients who were older than 70 years old and one was died. There was multiple sclerosis(MS) in one patient who had frequent attacks and interestingly patient had no attack after ruxolitinib. No thrombotic event was observed. Only one patient could not tolerate ruxolitinib. Patients who had PV did not need phlebotomy anymore.

Conclusion: All patients in our study responded to ruxolitinib treatment. Ruxolitinib is a feasible option with a high response rate for both PV and ET patients who were resistant or intolerant to previous therapies. It was well tolerated in our patients. Because our follow up period was short it is difficult to estimate the long-term efficacy of ruxolitinib. When using ruxolitinib in elderly patients it is suggested to be alert about serious infections.

PP-44

Two different myeloproliferative neoplasms due to JAK2V617F mutation of two siblings

A. Turgutkaya, İ. Yavaşoğlu, Z. Bolaman, İ. Erdoğdu, G. Bozkurt, F. Döğer
Adnan Menderes University

Background: Myeloproliferative neoplasms (MPN) usually develop because of acquired somatic stem cell driver mutations (JAK2, CALR, MPL) resulted from clonal expansion of myeloid precursors. This shares similar mechanisms in familial cases; it has been advocated that germline defects, although not illuminated completely, lead to acquire oncogenic mutations with time. Here we present two siblings, each diagnosed JAK2 (+) polycythemia vera (PV) at different times and transformed to post-PV myelofibrosis (Post-PV MF) and systemic mastocytosis associated with hematologic neoplasms (SM-AHN) respectively.

Case report: Case 1: Forty-eight-year old male patient was followed with JAK2V617F (+) PV diagnosis (detected by RT-PCR melting curve method, variant allele frequency 31%) since 2016, with the treatment of aspirin 100 mg/day and phlebotomy. His constitutional symptoms, which were absent at the time of the diagnosis, increased gradually, thus hydroxyurea 1 g/day was added to his treatment. During the follow-up, his spleen size progressed from 15 cm to 20 cm. His blood count showed the values Hb17.1 g/dl, Wbc 8260/mkrL, Neu 6040/mkrL, Eoz 480/mkrL, Baz 230/mkrL. Bone marrow biopsy was performed and SM-AHN was diagnosed by detecting more than 15 spindle shaped atypical mast cell aggregates. C-kit mutation and triptaz level results are awaited and the patient's follow-up and treatment still continues at our center.

Case 2: Fifty-six-year old female patient is the elder sister of the first case. She was followed with JAK2V617F (+) PV diagnosis (detected by RT-PCR Melting Curve method, heterozygous mutation) since 2005, and treated with aspirin 100 mg/day. She also received hydroxyurea 3 g/day and anagrelide 4 g/day because of resistant trombocytosis. Her spleen size progressed from 2 cm under the 12th costa midclaviculary to 20 cm. Her blood film showed 1% of blast,thus bone marrow biopsy was performed and showed the fibrous tissue content was grade 3 consistent with Post PV MF. Her DIPPS plus score was calculated as Intermediate-2 and Ruxolitinib 30 mg/day treatment was started. The patient's follow-up and treatment still continues at our center.

Discussion: It is advocated that 6–7% of MPN cases, which was considered initially sporadic, is reported as actually familial later. It also suggested that any relative of a MPN patient has a risk of MPN development 5–7 times more than the normal population. Some germline mutations and duplications such as ATG2B, GSKIP, RBBP6, SH2B3 were reported to cause familial MPN, although they are quite rare and incapable of illuminating the pathogenesis for other cases. The strongest relationship was found at JAK2 46/1 haplotype. Also, the single nucleotide polymorphism detected at telomerase reverse transcriptase gene (TERT) is another predisposing factor affecting the development of familial MPN. When 2 MPN cases were diagnosed in a single family, it's not recommended to screen the driver mutations among the rest of the other healthy family members, only to detect an asymptomatic MPN phenotype; although screening with blood count seems acceptable. The suitable examination was started to our patients' siblings accordingly.

Conclusion: It is important to keep in mind that MPN could be familial. It is essential to perform more clinical trials involving familial MPN cases to obtain early diagnosis, predict MPN types and prevent the complications of the siblings and relatives.

PP-45

Correlation of PET-CT with bone marrow biopsy to evaluate bone marrow infiltration in HL case series

A. Yetişir, M. Büyükşimşek, M. Tohumcuoğlu
Cukurova University Faculty of Medicine Dep of Medical Oncology

Objective: Hodgkin lymphoma (HL) accounts for approximately 0.5% of new cancers and 10% of lymphomas. HL is divided into two groups as classical (cHL) and nodular lymphocyte predominant HL (NLPHL). cHL is divided into four groups as nodular sclerosis (NS), mixed cellularity (MS), lymphocyte rich (LR) and lymphocyte depleted (LD). The prevalence of bone marrow infiltration (BMI) in HL is 4–18%. In HL, bone marrow biopsy (BMB) is used for staging. Since BMB is an invasive and painful procedure, positron emission tomography (PET-CT) has recently been described as an important tool in optimizing staging. The aim of this study was to compare the BMB and PET-CT in BMI.

Methodology: Of the 110 patients included in the study, 70 (64%) were male and 40 (36%) were female. The mean age of the patients was 37.45 (18–79) years. NS in 83 (75.45%), MS in 17 (15.45%), NLP in 7 (6.36%), LD in 2 (1.82%) and LR subtype in 1 (0.91%) patients was detected. 7 patients (6.36%) stage 1, 28 (25.45%) stage 2, 52 (47.27%) stage 3, and 23 patients (20.91%) had stage 4 disease. 110 patients followed in our clinic with the diagnosis of HL were evaluated retrospectively. The patients who underwent BMB and PET-CT for staging were evaluated. BMB was taken as the gold standard method in staging and the results were correlated with PET-CT.

Results: BMB was positive in 13 of 110 patients (11.81%), whereas it was negative in 97 patients. Of the 110 patients, 49 were positive for PET-CT (44.54%) and 61 were negative. While 11 patients were positive for BMB and PET-CT, 59 patients were negative. PET-CT was positive in 38 patients with negative BMB. PET-CT was negative in 2 patients with positive BMB. While 64% (n=70) of all patients were compatible with BMB and PET-CT, 36% (n: 40) were incompatible. PET-CT sensitivity was 84%, specificity was 60%, positive and negative predictive values were 22.4% and 96.7% respectively.

Conclusion: Staging is needed to determine treatment strategies in HL. BMB, which is the gold standard method for detecting BMI, is an invasive and painful procedure. In recent years, BMB has been replaced by PET-CT. In our study, PET-CT was evaluated as the BMI in 11 (10%) patients who were diagnosed with BMI by BMB. 38 (34.5%) patients with negative BMB interpreted PET-CT as false positive. PET-CT gave false negative results in 2 patients (1.8%) who were positive for BMB. BMB and PET-CT in HL should be considered as complementary tests to determine BMI. HL still maintains its importance in staging.

PP-46

The results of treatment with the use of different generations of tyrokinases in patients with CML in the Kyrgyz Republic

S. Zhusupova
National Center of Oncology and Hematology

Objective: Since 2003 at the National Center of Oncology and Hematology have been treated 301 patients with CML patient with chronic, acceleration and blast crisis phases. All patients received Imatinib from 2003 to July 1, 2019. Nilotinib received by 14 patients with acceleration phase and in blast crisis receive Ponatinib.

Methodology: Overall survival for 14 years was 85%. The death rate was 5.8%. The total cytogenetic response in the general group was 88%. The frequency of large molecular response and full molecular responses was 47% (116/254) and 35% (85/254), respectively. 221 patients are alive and continue to receive Imatinib therapy. The overall 5-year survival of patients was 86.4%, 10 year - 67.5%. For the first time in Kyrgyzstan, when monitoring a molecular genetic study in patients with resistance to the use of Imatinib at different stages of therapy a mutation was found: Y253H, E 255 G/C, F359V/c, T315A, T3151. In the presence of a positive analysis of bcr-abl and mutation Y253H, E 255 G/C, F359V/c in 4 patients since June 2017 at the expense of the MAX Foundation in Kyrgyzstan introduced second-generation drugs like Dasatinib, in which 2 patients who were in the blast crisis stage received a complete clinic hematological remission with 140 mg Dazatinib. 16 patients with the T3151 mutation received the 3rd generation drug Ponatinib. 13 patients were in the chronic phase, 4 patients were in the acceleration stage, 2 in the blast crisis stage and 3 had resistance to Gleevec in the chronic phase.

Results: All patients have an achievement of clinical and hematological remission on the background of only the use of Ponatinib. Side effects associated with the use of Ponatinib were like bone pain, weakness for 1 month. The spectrum and frequency of side effects of therapy were generally consistent with clinical studies.

Conclusion: The use of different generations of tyrosine kinase inhibitors in CML can significantly increase the duration and quality of life of patients. The use of Dasatinib and Ponatinib with Imatinib intolerance or resistance to it can be effective in most CML patients. Mutations of the BCR-ABL gene are one of the causes of resistance to Imatinib therapy of CML patient with CP. The lack of treatment correction based on mutational status can lead to CML progression.

PP-47

Localized skin edema associated with ATRA in a patient with acute promyelocytic leukemia: a case report

B. Sağlam, M. Albayrak, A. Yıldız, M. Tığlıoğlu, P. Cömert, Ç. Pala Öztürk, S. Maral, H. Afacan Öztürk, O. Şahin
University of Health Sciences, Diskapi Yildirim Beyazit Training and Research Hospital, Department of Hematology, Ankara, TURKEY

Background: Acute myeloid leukemia (AML) is a hematopoietic cancer originating from the myeloid series. Acute promyelocytic leukemia (APL) is a different variant of AML biologically and clinically and is classified as AML M3 by FAB classification and acute promyelocytic leukemia associated with PML-RARA according to 2016 WHO current classification. Life without treatment is shorter than 1 month. APL is a hematological emergency because it can cause hemorrhage, which can result in high mortality. Initiation of all-trans retinoic acid (ATRA) in early return has a very important role in reducing bleeding complications. Drug-related headache, fever, fatigue, generalized edema, skin rashes can be seen in most patients under ATRA treatment. Here we present a case of ATRA-related localized edema.

Case report: In December 2017, the patient presented with fatigue and nosebleed. After bone marrow aspiration and biopsy, flow cytometric examination and cytogenetic examination, APL was diagnosed. Induction chemotherapy was started with ATRA. ATRA was discontinued on the 31st day after localized edema, swelling and congestion in the face. Dexamethasone and antihistamine treatment was started. The patient was evaluated by the dermatology department and topical steroid was added to his current treatment and his complaints regressed. The ATRA treatment was interrupted for about 2 weeks and the patient's symptoms completely resolved. Afterwards, ATRA treatment was started again, firstly lower dose and full dose, and the patient was given first consolidation therapy. ATRA treatment was started for the second time and hyperemia and edema developed on the 37th day. After the complaints could not be controlled with steroid and antihistamine treatments, ATRA treatment was discontinued for the second time. Complaints of the patient regressed after discontinuation of medication with topical steroid and antihistamine administration. The treatment was continued with Arsenic Trioxide because the patient could not tolerate ATRA and control bone marrow biopsy was 7-8% blast. The patient did not repeat similar complaints during the next treatment period and is still being followed up in molecular remission under maintenance therapy.

Conclusion: Although ATRA is an effective and groundbreaking molecule in the treatment of APL, it has serious side effects. One of the most important side effects of ATRA syndrome is especially common edema. In our case, ATRA-related localized edema was a rare side effect. Further studies are needed to prevent such side effects and explain mechanisms.

PP-48

The patient who developed PRES after allogeneic stem cell transplantation

A. Eser, A. Timurağaoğlu
Hisar Intercontinental hospital

Background: Posterior reversible encephalopathy syndrome (PRES) is a kind of clinical situation that can be diagnosed only by neurologic examination and radiological imaging methods. Symptoms such as headache, changes in mental status, visual disturbances, paresis, nausea and generalized seizures may occur rapidly or gradually over several days and usually accompanied by hypertension. It was previously reported that eclampsia/preeclampsia, solid organ transplantation, immunosuppressive therapies, systemic inflammatory response syndrome, autoimmune diseases, porphyria, chemotherapy treatments and septic shock may trigger the PRES. Computed tomography (CT) and/or magnetic resonance imaging (MRI) shows extensive edema especially on the parietal and occipital lobes and this is the only radiologic finding in most patients. Because there are nonspecific clinical and radiological findings in the syndrome, this condition can often be confused with other disease may lead to unnecessary and/or incorrect treatments. In cases of early diagnosis and treatment, patients recover completely within a few weeks. Otherwise, the clinical condition may progress to ischemia, massive infarction or even death. We wanted to draw attention to a situation that could result in death if not treated carefully with this case by presenting our patient who developed PRES after allogeneic stem cell transplantation.

Case report: After busulfan-melphalan conditioning regimen, allogeneic stem cell transplantation was performed on 54-year-old female patient, who was diagnosed as acute myeloid leukaemia and resistant to induction therapy and partially responding to FLAG-IDA salvage therapy, from her full-match sister. After the transplantation, on day +17 neutrophil engraftment and +20 thrombocyte engraftment was detected. On the 31st day, the patient developed acute hepatic graft versus host disease and prednisolone 2 mg/kg was started. Next day recurrent tonic clonic epileptic seizures became evident. Although diazepam and levetirasetam were administered to the patient, her seizures could not be taken under control and then she was taken into the intensive care unit, sedated and endotracheal intubation was performed. Central nervous system (CNS) MRI revealed bilateral lesions on the frontal lobes. These lesions were firstly considered as leukemic involvement by the radiologist. The patient was awoken up at the end of the week and seizures did not relapse during the follow-up. The patient was consulted to the radiation oncologist and he was reported that this condition was PRES, not a leukemic involvement. Lesions regression was observed in the CNS MRI re-examination. The patient was discharged after her general condition became stable. However, seizures of the patient reoccurred at home and the patient was taken into intensive care unit at a hospital near her home. The patient died while being followed-up there.

Discussion: PRES is a kind of syndrome that its clinical and radiological findings can be rapidly reversed with rapid diagnosis and treatment. The clinical presentation may show similarities to many other neurological diseases. Encephalitis, ischemic or haemorrhagic cerebral events, demyelinating diseases, basilar artery embolism or cerebral venous sinus thrombosis should be kept in mind in the differential diagnosis. For treatment the first step is to remove the etiologic event if it is possible. The prevention of hypertension and factors that are thought to trigger the event (cytotoxic events, immunosuppressive drugs, sepsis, etc.) is the key point. Antiepileptic and antiedema therapy should be promptly begun. The etiology was probably immunosuppressive drugs in our patient. Cyclosporine and methotrexate was started before transplantation and continued subsequently, after the signs of hepatic GVHD prednisolone was added as third immunosuppressive drug to our patient during the transplantation period.

Conclusion: In conclusion, PRES is a condition that has multifactorial etiology, may reveal with different clinical findings and can be confirmed by radiological imaging methods. With early diagnosis, the disease can be reversed without sequalae. In our patient, rapid diagnosis of PRES and continuing the medical treatment under intensive care unit conditions positively affected the survival. The aim of this case report is to call the attention to the PRES syndrome if there are neurologic disturbances in transplantation patients.

PP-49

Richter transformation in patients with chronic lymphocytic leukemia: three cases and literature review

P. Cömert, M. Albayrak, A. Yıldız, M. Tığlıoğlu, B. Sağlam, O. Şahin
Diskapi Yildirim Beyazit Training and Research Hospital, Department of Hematology, Ankara, TURKEY

Background: Richter syndrome (RS) is defined as the transformation of chronic lymphocytic leukaemia (CLL) into an aggressive lymphoid malignancy. The incidence of RS varies from 1% to 9% and it is generally characterized by an aggressive clinical course. The cases are here reported of 3 CLL patients with RS and their clinical outcomes.

Case report: The first case was a 44-year-old male patient was diagnosed with CLL and had received chemotherapy because of lymphadenopathy causing compression and B symptoms. After treatment, complete remission was achieved. 3 years later of CLL diagnosis, RS was developed with a mass lesion in nasopharynx and involvement of cerebrospinal fluid.

The second case was a 66-year-old female patient with CLL who did not need treatment, a mass lesion was detected in 8th months after diagnosis and true-cut biopsy from the mass showed DLBCL transforming on the background of CLL.

The third case was a 77-year-old male patient who was diagnosed as stage-2 CLL. After 18 months (30 months after diagnosis) exacerbation of B symptoms and symptomatic splenomegaly was developed and para-esophageal 72 mm mass lesion in the thorax were detected. A true-cut biopsy of the present mass lesion was reported as DLBCL transforming on the CLL background.

Conclusion: The results of these cases suggest that RS is a rare and heterogeneous condition characterised by an aggressive presentation, with low treatment response rates and very poor survival. RS should be considered in patients with clinical exacerbation such as the development of B symptoms, enlargement of lymph nodes especially during follow-up after 2 years from diagnosis

PP-50

Renal involvement in chronic lymphocytic leukemia: a case report

S. Demircioğlu[1], M. Özgökçe[2], A. Doğan[3], İ. Bayram[4], C. Demir[3]
[1]Necmettin Erbakan University, Meram Faculty of Medicine, Department of Hematology; [2]Van Yüzüncü Yıl University, Faculty of Medicine, Department of Radiology; [3]Van Yüzüncü Yıl University, Faculty of Medicine, Department of Hematology; [4]Van Yüzüncü Yıl University, Faculty of Medicine, Department of Pathology

Background: Chronic lymphocytic leukaemia (CLL) is a neoplastic condition of B cells that frequently affects the lymph nodes, liver, spleen and bone marrow. The extranodal involvement of CLL is most commonly observed in the skin, whereas gastrointestinal and genitourinary involvement is rare. Renal involvement may not always present with renal failure.
Case report: A 63-year-old male patient was being followed up with a diagnosis of Stage 2 CLL since 2016. The patient complained of night sweats for several years. Physical examination revealed cervical, axillary and inguinal lymphadenopathies (LAP) that were painless, soft and mobile, with the largest being 2 cm in diameter. In addition, masses of 3–5 cm were palpated on the liver and spleen and under the ribs. Leukocyte count was 44,160/mL, lymphocyte count was 32,870/mL, haemoglobin level was 12.40 g/dl, platelet count was 272,120/mL, creatinine was 1.14 mg/dl and LDH was 189 U/L. Complete urinalysis did not reveal proteinuria. The results of bone marrow biopsy were suggestive of CLL. In the genetic examination, 90% of the analysed cells had a deletion in the 13q14.3 region, and 11q22.3, trisomy 12, 17p13.1 deletion and p53 mutation were not observed. Abdominal ultrasonography (USG) revealed hepatosplenomegaly, LAPs in the abdomen and a heterogeneous lesion (17 mm in diameter) in the left kidney upper pole. Abdominal computed tomography (CT) revealed a hypodense lesion of approximately 22 × 18 mm, with a mean density of 69 Hounsfield units in the left kidney upper pole posterior. Needle biopsy was performed on this lesion, and the following results were reported: CD20(+), CD5(+), CD23(+), Bcl2(+), CD3(−), CD10(−), Bcl6(−), cyclin D1(−), TdT(−) and Ki67 proliferation index was 5%. A diagnosis of CLL/SLL was made. The overall condition of the patient was good, with an Eastern Cooperative Oncology Group (ECOG) performance score of 1. Thus, rituximab–bendamustine chemotherapy was started.
Discussion: The most common imaging finding of renal involvement in leukaemia is nephromegaly, which can affect one or both kidneys and is caused by widespread or nodular parenchymal infiltration of leukaemic cells. However, the sensitivity and specificity of this finding remain unknown. For example, nephromegaly was detected only in 1 of the 10 patients with proven renal infiltration on biopsy. Obstructive uropathy can also be observed in CLL. Diagnosis can be made using imaging methods, such as USG, CT and magnetic resonance imaging.
Conclusion: Renal involvement is rarely observed in CLL. Each case of renal insufficiency observed in CLL may not be related to infiltration. Post-renal renal insufficiency due to paraneoplastic syndromes, tumour lysis syndrome, chemotherapy-related toxicity and lymphadenopathies should not be overlooked.

PP-51

Successful treatment of transplant-associated thrombotic microangiopathy with eculizumab

S. Demircioğlu[1], A. Doğan[2], C. Demir[2]
[1]Necmettin Erbakan University, Meram Medical Faculty, Department of Hematology; [2]Van Yüzüncü Yıl University Medical Faculty, Department of Hematology

Background: Transplant associated thrombotic microangiopathy (TA-TMA) is endothelial damage syndrome identified as a complication of both autologous and allogeneic hematopoetic cell transplantation (HCT). It is a disease with high mortality often experienced in the first 100 days. Although its etiology is not clear, drugs, radiotherapy, graft-versus-host disease (GVHD) and angioinvasive fungal or viral infections are generally blamed. Furthermore, complement mutations and uncontrolled complement activation are also included in the etiology.
Case report: Forty-six-year old female patient was diagnosed with AML on July 2017. One course of remission induction chemotherapy and 4 courses of consolidation chemotherapy were administered, and drug-free follow up was started. A relapse was experienced 9 months after the last chemotherapy on September 2018. Remission was induced with rescue chemotherapy, and allogeneic stem cell transplantation was performed to the patient on October 2018 from a full-matched donor, her brother. The patient experienced gastrointestinal GVHD on the 155th day of transplantation. She was successfully treated with methyl prednisolone and cyclosporine. Methyl prednisolone and cyclosporine were stopped at +180th day. The patient has applied with the complaint of fatigue on +195th day, and the following results were determined: hemoglobin 8.3 g/dl, leukocyte count 4420/μL, platelet count 29,000/μL, creatinine 0.8 mg/dl, AST 57 U/L, ALT 94 U/L, CRP 6 mg/L, LDH 1,072 U/L, GGT 175 U/L, ALP 172 U/L, indirect bilirubin 1.8 mg/dl, INR 1.1, PT 12 sec, APTT 30 sec, fibrinogen 328 mg/dl, D-dimer 0.4 μg/ml. Schistocytes, spherocytes, polychromasia and thrombocytopenia were observed in peripheral smear (PS). ADAMTS 13 enzyme level was determined as 1 IU/ml (0.40–0.30). No PNH clone was detected. Bone marrow examination revealed that the disease was in remission. Plasmapheresis and 1 mg/kg methylprednisolone treatment was started in the patient since transplant associated thrombotic microangiopathy was considered. Fourteen sessions of plasmapheresis were performed. However, no treatment response could be obtained. Eculizumab treatment was planned. Eculizumab was administered at 900 mg once a week dose in the first 4 weeks, then 1,200 mg dose was applied once in two weeks. Clinical and laboratory recovery started after the second dose of eculizumab treatment. After the sixth dose of eculizumab, hemoglobin level increased to 12.2 g/dl and platelet count increased to 154,000/μL, while LDH level decreased to 205 U/L and indirect bilirubin decreased to 0.8 mg/dl. Schistocytes in the peripheral smear have disappeared.
Discussion: TA-TMA treatment is mostly supporting. At the first line therapy, calcineurin inhibitors such as tacrolimus, sirolimus and cyclosporine, which are considered to be possibly responsible for the development of TMA, should be stopped, if possible, or their doses should be reduced. Therapeutic plasma exchange, steroid and rituximab are treatments that are preferred first. Eculizumab, which is a complement inhibitor, has been used successfully in some TA-TMA cases. While our patient did not respond to steroid and therapeutic plasma exchange, she responded dramatically well to eculizumab treatment.
Conclusion: Eculizumab should be kept in mind as a treatment option that may be used in TA-TMA treatment.

PP-52

The incidence of venous thromboembolism in post-bariatric surgery patients

T. Alshuaıbı[1], N. Alobaıdı[1], A. Almutawa[1], H. Basunbl[1], F. Almarshed[2], M. Almegren[3]
[1]King Fahd Hospital, Jeddah; [2]Shagra University; [3]Alimam Mohammed Ibn Saud Islamic University

Background: Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common cause of morbidity and mortality after bariatric surgery. The published data in bariatric surgery have suggested a VTE incidence of 2.4%, PE incidence of 0.2-0.3%, and a 30-day mortality rate of 0.1–2%. One study reported the LMWH is an extended VTE prophylaxis regimen is simple and effective to prevent VTE events after bariatric surgery.
Objective: To evaluate the incidence of VTE in post-bariatric surgery patients.
Methodology: Using the resources of the electronic health records of King Fahad General Hospital in Jeddah, Saudi Arabia, we identified all patients with incident VTE after undergoing bariatric surgery from March 2012 through August 2018. Using the Kaplan-Meier estimator we determined the cumulative incidence of VTE after bariatric surgery. JASP statistic software was used to assess the patients demographic characteristics.
Results: We identified 374 patients who underwent bariatric operations. The most common operation was a laparoscopic gastric sleeve (n=357).

Two patients had VTE event after bariatric surgery includes proximal deep vein thrombosis. VTE events occurred after 21 days and 70 days of hospital discharge. The cumulative incidence of VTE in post-bariatric surgery patients was 0.53% (95% CI, 0.45–0.60). The most used pharmacological prophylaxis (91%) for the prevention of VTE after bariatric surgery was Enoxaparin 40 mg BID for the two weeks after hospital discharge (n=340). The prevalence of bariatric surgery in female patients was 73%, the median age was 35 years. The median follow-up time was three months. There was no bleeding events was identified.

Conclusion: Bariatric surgery is now a common and effective method of obesity treatment. Our study revealed the low VTE incidence and no risk of bleeding in the patients after bariatric surgery. The benefits of extended outpatient thromboprophylaxis is warranted in patients undergoing bariatric surgery to prevent VTE

PP-53

Studying the problems of connected pathological condition of the liver in children with acute lymphoblastic leukemia

M. Babayev, K. Mehtiyeva, A. Ahmadova, N. Babayeva
Institute of Hematology and Transfusiology

Objective: This research work is devoted to studying the problems of the liver during the debut and at the stage of induction therapy of acute leukemia in children. The relevance of the work is associated with organic and functional disorders of the liver in leukemia, which is based on leukemic, toxic and virological factors of damage.

Methodology: The study group included 110 patients aged from 9 months. up to 15 years with primary acute lymphoblastic leukemia. The work was carried out in the children's department of the Research Institute of Hematology and Transfusiology of Azerbaijan. The data obtained showed the following:

Results: In the debut of ALL, leukemic liver damage was found in 74.6% of patients. Serious organic changes were noted in 34.5% of cases, and in 8.1% of patients it was accompanied by functional organ lesions. Against the background of initiated chemotherapy, these changes disappeared within the first two weeks. Toxic liver damage (toxic hepatitis) associated with the use of cytostatics was observed in 90% of patients at the stage of induction of remission and it was more pronounced in the second and third decades of the course. The correct choice of treatment for hepatitis in all cases led to a complete recovery from this disease. Cases of hepatitis viral etiology are not reported in any case in the debut and at the stage of induction therapy of leukemia.

PP-54

The course of acute leukemia in a patient with Down syndrome

M. Babayev, K. Mehtiyeva, A. Ahmadova, N. Babayeva
Institute of Hematology and Transfusiology

Background: The incidence of leukemia among patients with Down syndrome is significantly ahead of the normal population. This is based on the presence of a congenital chromosomal defect, trisomy of the 21st chromosome. And on the other hand, the onset of leukemia directly depends on the resistance of the chromosome apparatus. Hence comes the frequency of occurrence of two serious ailments in the same patient. Without treatment, these patients are considered to be sentenced to death. And to treat them, there was always a skeptical attitude because of the psychological and difficult to accept chemotherapeutic aspect. Therefore, we usually refused to treat leukemic children with down syndrome. And it was the mutual desire of the parents. But the recent case has changed our view on this issue.

Case report: Our clinic received a girl in a serious condition at the age of 3 years with Down syndrome. The severity was due to anemia (Hb 36 g/l) and numerous hemorrhagic manifestations. Based on the obtained laboratory data, the diagnosis of acute lymphoblastic leukemia, L1, B-cell variant was established. At the insistence of parents, we decided to treat leukemia. To do this, we chose the program "Moscow – Berlin 2002 ImRG". Given the age and severity of the patient's condition, as well as our skeptical attitude to the final positive result, it was decided to conduct a course of induction only with dexamethasone, as a monotherapy. Against the background of the chosen tactics, a gradual improvement in the clinical and hematological condition was noted. By the 15th day in the bone marrow the number of blast cells decreased from 96.6% to 35%, and by the end of the induction course, on the 36th day it was 2.8%. Thus, clinical and hematological remission was achieved. In the future, we decided to conduct treatment in full, i.e. to carry out chemotherapy at the request of the program. The patient received 3 courses of consolidation and maintenance therapy. In total, the treatment lasted 2.5 years. The achieved clinical and hematological remission remained until the end of treatment and on the last day of blast cells in the bone marrow was 0.8%. It took 4 years after treatment. For all this time the girl was under our observation and her health remained normal. At the moment, the child receives rehabilitation therapy for psycho - motor development.

Conclusion: Thus, the result showed us that it is necessary to treat leukemic patients with Down syndrome more optimistically and individual approach to the choice of treatment tactics.

PP-55

Behçet's disease and T-cell large granular lymphocytic leukemia: two case reports

G. Tazegul[1], Ü. Ataş[1], O. Yücel[1], O. Salim[1], V. Yazısız[2], L. Ündar[1]
[1]Akdeniz University Faculty of Medicine, Department of Hematology; [2]Akdeniz University Faculty of Medicine, Department of Rheumatology

Background: T-cell large granular lymphocytic leukemia (T-LGL), a clonal proliferation of cytotoxic T-cells, is a rare disorder characterized by a chronic course and cytopenias. Most patients present with co-existing autoimmune disorders, most commonly rheumatoid arthritis. Sjögren's syndrome, systemic lupus erythematosus, ulcerative colitis and multiple sclerosis are also reported. Behçet's disease (BD) is a chronic inflammatory disorder with recurrent oral and genital ulcers, uveitis, other systemic findings such as neurologic involvement, vasculitis and arthritis. Pathogenesis of BD is still poorly understood. However, a polarization of the Th1/Th2 immune response toward the Th1 pathway has been shown in active BD. In these case reports, we present two cases of T-LGL with BD.

Case report: Case 1: A 21-year-old female patient was previously diagnosed with T-LGL 3 years ago with splenomegaly and bicytopenia (anemia and neutropenia) and lymphocytosis. She was splenectomized to increase quality of life. For three years, she was asymptomatic. She was admitted with recurrent oral and genital aphtous ulcers. She also had arthralgia, an episode of uveitis and two episodes of pleurisy. She had been treated with methylprednisolone plus colchicine for BD, however, colchicine was stopped due to liver enzyme elevation. At admission, blood smear and flow cytometry was consistent with T-LGL. A liver biopsy to diagnose any concurrent autoimmune liver disease showed only T-LGL infiltration. A workup for other autoimmune diseases revealed a co-existent myasthenia gravis as well. She has been treated with oral cyclophosphamide and pyridostigmine, and both her symptoms and liver enzymes gradually improved.

Case 2: A 55-year-old female patient was referred with oral and genital ulcers, fever, leukopenia and arthralgia. She had BD for five years previously. She was treated with prednisolone and colchicine. Laboratory results showed a hemoglobin of 10.9 g/dL, a white blood cell count of 2,200/mm^3 with 9% neutrophils and 72% lymphocytes. During follow-up, piperacillin/tazobactam was administered for febrile neutropenia. Patient exhibited rapid resolution of systemic symptoms after 7 days of antimicrobial therapy, but neutropenia and lymphocytosis continued. Blood smear revealed atypical lymphocytes constituting 75% of the white blood cell population. Blood smear and flow cytometry was consistent with T-LGL. Patient was treated with methylprednisolone and methotrexate; her symptoms and cytopenias gradually improved.

Conclusion: Herein we report two cases with co-existing BD and T-LGL. As far as we know, these case reports are the second and third cases in the literature. In the previous case report of T-LGL and BD co-existence, authors have found that FasL and IL-18 levels were extremely high in patient serum. They suggested that FasL and IL-18 produced by CD8(+) T-LGL cells might play a role in the immunopathogenesis of BD as well. Severe neutropenia,

symptomatic anemia or thrombocytopenia, severe constitutional symptoms and co-existing autoimmune diseases are the most common indications for therapy in T-LGL. In the present cases, both patients gradually improved with treatment, highlighting a possible pathogenetic link between the two diseases. In conclusion, with these two unique cases, we would like to emphasize that there may be a pathogenetic association between BD and T-LGL.

PP-56

Risk factors for invasive fungal infection in patients who underwent allogeneic hematopoietic stem cell transplantation

E. Yildizhan[1], F. Varal[2], S. Ciftci[2], E. Coskun[2], G. Yildiz[2], A. Yanar[2], B. Eser[2], M. Cetin[2], L. Kaynar[2], A. Unal[2]
[1]Kayseri City Hospital, Hematology Department; [2]Erciyes University, Faculty of Medicine, Hematology Department

Objective: This study was conducted in order to define the frequency and potential risk factors for invasive fungal infections (IFI) in patients who underwent allogeneic hematopoietic stem cell transplantation (AHSCT).
Methodology: We retrospectively reviewed data from 54 patients who underwent AHSCT in Erciyes University Hematology and Bone Marrow Transplantation Center between January, 2017 and February, 2018. After transplantation, with diagnose based on EORTC/MSG criteria, first invasive fungal infection episode was noted. Patients were divided in two groups regarding the presence of IFI (IFI positive and negative) and potential risk factors were compared in these two groups. For mucositis, vomiting and parenteral nutrition the cases within one week before diagnosis of IFI were noted.
Results: IFI were detected in 17 (31.5%) of 54 patients. All of the patients received antifungal prophylaxis until 75th day of transplantation (with posaconazole for acute leukemia patients and with fluconazole for others). Neutrophil engraftment was failed in 6 (35.3%) of IFI positive patients and in one (2.7%) of IFI negative patients ($p<0.01$). When these engraftment-failed patients excluded, neutrophil engraftment times were 15.6±4.5 and 17.4±3.6 days respectively ($p=0.19$). In terms of mucositis and vomiting; the two groups are not significantly different but parenteral nutrition is significantly high in IFI positive patients (88% vs 43%; $p=0.002$).
Conclusion: In conclusion; invasive fungal infections are still an important problem for hematopoietic stem cell recipients and may occur despite prophylaxis. Many factors may affect development of IFI and some of them may be avoidable or improvable.

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A relapsed refractory CD30 positive cutaneous anaplastic large cell lymphoma with large B-cell transformation responding to brentuximab vedotin after multiple lines of treatment

S. Erdem[1], M. Özbalak[1], C. Baykal[2], S. Kalayoğlu Beşışık[1]
[1]Istanbul University Istanbul Faculty of Medicine, Internal Medicine Department, Hematology Division; [2]Istanbul University Istanbul Faculty of Medicine, Dermatology Department

Background: CD30-positive cutaneous T-cell lymphomas (CTCLs) account for about 30% of CTCLs which include: lymphomatoid papulosis (LP), anaplastic large cell lymphoma (ALCL), and some cases of mycosis fungoides with large cell transformation (MFLCT). It often manifests itself as papules, nodules, or plaques. Lesions are usually solitary or few in number, generally restricted to a single anatomical area. However, it is estimated that 20% of patients have multifocal lesions. Primary cutaneous ALCL lesions tend to be fewer, larger, and slower. The lesions are usually asymptomatic with good prognosis as 10-year survival rate is approximately 90%. The lesions usually do not regress spontaneously and rarely the disease can be systemic.
Aim: We present a case of CD30-positive primary cutaneous ALCL with insidious onset but progressing associated secondary malignancies.
Case report: A 74-year-old male patient reported the appearance of nodular lesions on both of upper and lower extremities. Histologic documentation was consistent with cutaneous lymphoproliferative disease of T cell origin. Whole body examination revealed systemic involvement. Oral methotrexate (MTX) was started accompanied with radiotherapy to bulky lesions. The dissemination progressed and bulky lesions were gradually uncomfortable. That time combined chemotherapy protocol with cyclophosphamide, etoposide, vincristine, and methylprednisolone (COEP) of 6 courses was commenced and resulted complete response which lasted only 8 months. Due to cutaneous relapse, the disease was restaged which revealed gastric FDG activity with a SUDmax of 13 on PET-CT. Biopsy of gastric mucosa showed diffuse large B cell lymphoma. He received that time rituximab combined anthracyclin included protocol R-CHOP and achieved complete response with disappearance of all cutaneous lesions. After three years he relapsed as localized disease and treated with localized radiotherapy. At ninth year of cutaneous ALCL he relapsed as systemic disease with cutaneous involvement. Rebiopsy revealed CD30 positive ALCL. Brentixumab vedotin was started as 4th line systemic treatment. All cutaneous and mass lesions regressed but a little right preauricular lesion remained. The latter was removed and histologic documentation revealed basal cell skin carsinoma. The excision was sufficient and no additional treatment was given. After one year he was re-evaluated due to severe headache and cranial MRI showed a mass lesion consistent with meningioma. No treatment change was made. Brentixumab vedotin with bendamustin treatment was continued at least of 16 courses with a decision until relapse or toxicity
Conclusion: ALCL is a CD30-positive non-Hodgkin's lymphoma, classified by the World Health Organization as primary ALCL cutaneous and systemic ALCL. ALCL affects more young adults and is two to three times more common in men. As a rare presentation our patient was an elderly patient and had systemic progression. Combined chemotherapy protocol was used for rapidly progressive course and bulky cutaneous involvement. Brentuximab vedotin - an anti-CD30-auristatin-E/monomethyl antibody-drug conjugate - has been approved for use in relapsed CD30-positive Hodgkin's lymphoma and systemic ALCL. Its use with CD30-positive CTCL patients looks promising, but further studies are needed to establish its indication to clinical practice

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Impact of myeloproliferative neoplasms (MPNs) and perceptions of treatment goals amongst physicians and patients in 6 countries: an expansion of the MPN landmark survey

G. Saydam[1], C. Chang[2], E. Morozova[3], S. Bang[4], M. Alzahrani[5], K. Mycock[6], I. Rajkovic[6], A. Siddiqui[7], Z. Xiao[8]
[1]Ege University Hospital, Turkey; [2]Chang Bing Show Chwan Memorial Hospital, Taiwan; [3]St. Petersburg State Pavlov Medical University, Russia; [4]Seoul National University Bundang Hospital, South Korea; [5]King Saud University, Saudi Arabia; [6]Adelphi Real World, Bollington, United Kingdom; [7]Novartis Pharma AG, Basel, Switzerland; [8]Institute of Hematology & Blood Diseases Hospital, CAMS, China

Background: Previous surveys in North America, Europe and Japan have extensively documented the high symptom burden associated with myeloproliferative neoplasms (MPNs) such as myelofibrosis (MF), polycythemia vera (PV) and essential thrombocythemia (ET). No such data are available for the rest of the world. This study evaluated patient (pt)- and physician-reported perceptions of symptom burden, treatment goals and disease management.
Methodology: A cross-sectional survey of pts with MPNs and physicians treating pts with MPNs was conducted in China, Turkey, Russia, Taiwan, South Korea and Saudi Arabia. Independently recruited respondents completed an online survey measuring their perceptions of the impact of MPNs.
Results: 506 pts (52% female) completed the survey, with most patients experiencing symptoms for ≤1 year prior to MPN diagnosis (83%). 240 physicians completed the survey. At consultation, only 36% of physicians used a validated symptom assessment form; 39% used their own rating method. Many pts also did not recognize that their symptoms could be MPN-related. For example, fatigue/tiredness was one of the most commonly reported symptoms to physicians (69% MF, 40% PV, 54% ET) but many pts did not think their fatigue resulted from MPNs (18% MF, 25% PV, 18% ET). Consistent with this, physicians (43%) indicated that pts could only identify few/some of their symptoms as MPN-related. Over four-fifths of physicians (83%) reported that

even mild-moderate symptoms can have a negative impact on pts' quality of life (QoL). High proportion of physicians and pts felt that MPN symptoms have a negative impact on pts' QoL (91% and 83% respectively). Despite this, reducing MPN symptoms seemed to be a priority more for pts (72% MF; 68% PV; 68% ET) than physicians (61% MF, 43% PV, 55% ET), while more physicians than pts ranked a better QoL as key treatment goal. Slowing/delay in disease progression as a treatment goal was more common for physicians than pts in PV. As well as a high symptom prevalence, pts reported a substantial emotional burden associated with their disease: 78% MF, 59% PV and 57% ET pts were anxious/worried about their condition. Overall, a high burden on activities of daily living (ADL) was reported, especially in MF. Overall only 28% of physicians felt in complete agreement with their pts on treatment goals. One-quarter of patients were dissatisfied with their doctors understanding and support of treatment goals and patients reported often feeling worse than their physician was aware (62% MF; 42% PV; 47% ET). Interestingly, these patients still expressed their satisfaction (45–51% very satisfied) with their doctor's management and treatment of their MPN.

Conclusion: Study revealed lack of understanding of MPN symptoms among patients; physicians agreed that their pts could identify few MPN-related symptoms. Although physicians acknowledge adverse impact of symptoms on QoL, more patients than physicians see reducing symptoms as a treatment goal. Despite reported pt satisfaction in disease management, pt- physician disconnects are apparent, demonstrating a need for improved communication. A need for standardization in symptom assessment was also highlighted, which could result in improved pt understanding of MPNs. Results for Turkish dataset would be discussed.

PP-59

The impact of blinatumomab administration prior to allogeneic stem cell transplantation on the immune reconstitution post allografting

P. Kaloyannıdıs[1], N. Musaılem[1], S. Kanfar[2], H. Soudı[3], H. Al Hashmı[2], K. Al Anezı[2]

[1]Adult Hematology & Stem Cell Transplantation Department, King Fahad Specialist Hospital, Dammam, Saudi Arabia; [2]Adult Hematology & Stem Cell Transplantation Department, King Fahad Specialist Hospital, Dammam,Saudi Arabia; [3]Pharmacy Department, King Fahad Specialist Hospital, Dammam, Saudi Arabia

Objective: Blinatumomab, the bispecific CD19/CD-3 engager has been produced remarkable responses in patients with refractory/relapsed or with minimal residual acute lymphoblastic leukemia (ALL) and has been used as a bridge to allogeneic stem cell transplantation (alloSCT). However, there is lack of data regarding its effect on the long-term outcome post alloSCT. In this report we evaluated the long-term effect of blinatumomab on the engraftment process and immune reconstitution, in patients who received blinatumomab prior alloSCT. We analyzed the outcome of small case series of patients who received blinatumomab for 2nd salvage regimen, as "bridge" to alloSCT

Methodology: We retrospectively reviewed the medical records and the clinical course of 3 patients who received a median of 2 (1-2) cycles of blinatumomab for 2nd salvage regimen, as "bridge" to alloSCT. One patient was assessed with primary refractory disease while 2 patients with refractory relapsed ALL. No patient had poor risk molecular or cytogenetic abnormalities. All patients achieved hematological remission with MRD negativity pre-alloSCT. No toxicity >grade 3 were observed during blinatumomab administration. The median interval between Blinatumomab and alloSCT was 2 (2–3) months. T-cell repleted peripheral blood grafts of a median of 4.5×10^6/kg CD34+ cells were infused from full matched-siblings (2 patients) or from haploidentical (1) donors after a myeloablative (2) or reduced intensity (1)regimen. The GvHD prophylaxis was cyclosporine (CSP) plus short term methotrexate or mycophenolate mofetil (MMF) while post-transplant cyclophosphamide (PTCy) was given additionally to CSP+MMF in the haploidentical-allotransplant.

Results: The engraftment was successful and patients reached >500/mm^3 neutrophils and >25,000/mm^3 platelets at a median of +22 (19–24) and +13 (13–16) days, respectively. All patients achieved full donor originated hematopoietic chimerism after the +30 day. Two patients developed chronic GvHD and required prolonged immunosuppression treatment (CSP or MMF plus steroids). As it was expected, at the first trimester post-transplant, the B-cells were not detectable. However, after the 6th month a gradual B-cell recovery was noticed and finally the median B-cell counts at 9 and 12 months were 321 (111–908) and 577 (368–1594)/mm^3 respectively. The immunoglobulin levels also gradually increased after the 2st trimester, however all patients received regularly intravenously immunoglobulins during the first 6 months post-transplant. The T-cell recovery was also successful; CD4: 245 (75–416), 425 (193–658), 851(282–943) and 831 (662–922)/mm^3 cells and CD8: 692 (491–892),1815 (1142–2491), 2044 (1370–2245) and 2281 (1396–3061)/mm^3 cells and at +3, +6, +9 and +12 months respectively. During the 12 months period transplant, one patient developed grIII bacterial infection required treatment with IV-antibiotics while 2 patients developed viral infection (CMV- and VZV-infection) that successfully managed with specific antiviral treatment. Currently all patients after a median of 19(17-36) months post allografting are in complete remission and off any immunosuppressive treatment.

Conclusion: In our patients, Blinatumomab was effective in terms of disease control before alloSCT and showed a safe profile during the early and long-term post alloSCT period, not adversely affecting the engraftment, immune reconstitution and infections incidence.

PP-60

A regional hemovigilance study of transfusion-related adverse events at a university hospital from Istanbul

Ü. Kaftancıoğlu, Ç. Ateşmen, N. Yanık, M. Yanaşık, S. Kalayoglu

Istanbul Üniversity, İstanbul Medical Faculty

Objective: Approximately 0.5–3% of all blood transfusion results in adverse transfusion-related events without any major consequence. Hemovigilance Programme of Turkey was introduced on 20 April, 2015 by a Commission in association with Turkish Hematology Society. The aim of the program is to track adverse transfusion events and to know the pattern, introduce best practices and interventions for improving the patient safety and care while improving the overall health care. This study was conducted with the primary objective to evaluate the types and frequency of acute transfusion reaction (ATR).

Methodology: The study was a prospective observational study and pursued after obtaining ethics committee approval during April, 2015 to April 2019. All ATRs, reported to the blood bank, in hospitalized patients at Internal Medicine Clinics were recorded and assessed as per departmental standard operating procedures.

Results: During the 4-year study period, 19.402 units of blood components were issued. These comprised 4,231 (22%) packed red blood cells (RBC), 318 (1.65%) fresh frozen plasma (FFP) 7,415 (38%) random donor platelet concentrates, and 2,872 (15%) single donor apheresis. The ATRs reported to the department during the study period were 215/19,402 (2.5%). A total 215 ATRs developed in 166 patients whereas 35 of them experienced 86 times ATR. ATRs were observed in all age group patients. The ATRs were allergic urticarial 68.39%, FNHR 21.67%, anaphylactic reactions 1.39%, circulatory overload 3.18%, hemolytic 0.6%, and isolated hypotension 0.2%. No transfusion-related acute lung injury was recorded. In 2.98% of patients ATR type could not be determined.

Conclusion: The frequency of ATRs were found to be not striking higher rate. Allergic urticarial TRs were being the most common. We think the underestimation of the true incidence due to the underreporting can be improved by hemovigilance system. Adequate manpower with continuous medical education will strengthen patient blood management programs and hemovigilance system which will reduce the incidence of ATR.

PP-61

Red blood cell alloantibodies in thalassemia major patients: an analysis from Istanbul

M. Yanaşık[1], S. Kalayoğlu Beşışık[1], S. Karaman[2], D. Tuğcu[2], Z. Karakaş[3]
[1]Istanbul Üniversity, İstanbul Medical Faculty, Blood Center; [2]Istanbul Üniversity, İstanbul Medical Faculty, Department of Pediatric Hematology; [3]Istanbul Üniversity, İstanbul Medical Faculty,Department of Pediatric Hematology

Objective: Thalassemia occurs most often in African–Americans and in people of Mediterranean and Southeast Asian ancestry. Thalassemia, with approximately 1.300.000 carriers and 4.500 diseased population, is one of the most prevalent inherited blood disorder in Turkey. To correct anemia in the β-thalassemia major patients, regular blood transfusion regimen every 3–4 weeks was recommended that could lead to alloimmunization to red blood cell (RBC) antigens. Alloantibodies and/or autoantibodies of RBC that lead to difficulty in cross-matching and delay in obtaining compatible blood for transfusion are a serious problem in patient blood management of thalassemia. AIM: The study was conducted to know the prevalence of alloimmunization in thalassemia patients, admitted to İstanbul Medical Faculty, one of big hospital in Turkey.
Methodology: This study is a retrospective analysis of transfusion records of 111 patients with β-thalassemia major who received regular transfusions; transfusion dependent thalassemia (TDT). All patients had been routinely tested prior to transfusion for ABO and RhD antigens using gel/column agglutination test. The antibody screening test was performed using three/four cells sets (GRIFOLDS from 2006 to 2007; Ortho Clinical Diagnostics from 2007 to 2018; Across from 2018 to 2019) were used. All TDT patients have been matched for ABO, Rh (C, c, D, E, e) and Kell antigens and received leucodepleted red cell transfusion.
Results: 104 TDT patients (female; male; 61:43, median age: 26, ranges; 1–53 years) were included in the study. Fourteen patients were positive for alloantibodies (13.6%). Of them, 64.3% (9 cases) had only one alloantibody, and 35.2% (5 cases) had at least two or more of alloantibodies. The most prevelant alloantibodies were anti-E in 4 cases (10.5%) followed by both of anti-K and anti-Cw (5.2%) existence in 3 cases. Thirty-five patients (33.7%) developed autoantibodies. Five out of 14 patients with alloantibodies also had autoantibodies. Age of onset transfusion could not be determined due to interior migration in the country
Conclusion: There are some proposed risk factors for alloantibody development in thalassemia major patients such as multiple exposure to foreign red blood cells, especially ethnic disparities between the recipients and their blood donors and splenectomy. Alloimmunization rate what we found in our study was similar to that prior has been reported by various workers as 5–30%. Thalassemia major patients require lifelong transfusion support. Early at transfusion start extended phenotype matching and leucodepleted red cell transfusion might lead to some immune prevention of alloimmunization.

PP-62

Is prescribing acid suppressive drugs for every patient is a good decision: a pH+ all case report

A. Günay[1], Z. Güven[2], S. Çelik[2], M. Çetin[2], M. Aycan[1], E. Demirpolat[1], A. Ünal[2]
[1]Erciyes University, Faculty of Pharmacy; [2]Erciyes University, Department of Hematology

Background: Prescribing acid suppressant drugs is a common practice used to prevent patients from gastrointestinal symptoms that can occur due to use of co-medications. Especially patients with malignancy are exposed to many medications during their cancer treatment regimens. Drug-drug interactions are among major problem that can cause treatment failures. While it is crucial to take into account potential interactions for getting the desired effect from drugs physicians may not always be aware of the effect of those interactions on the success of the treatment. In recent years novel orally administered, molecularly targeted anticancer drug therapies have been introduced in oncology and hemato-oncology fields. These new drug class members are weak bases that shows pH-dependent solubility, thereby suppression of patient's gastric acidity with proton pump inhibitors, H2 receptor blockers or antacid supplements could impair their absorption and it results decreasing bioavailability of tyrosine-kinase inhibitors. Many studies suggest that drug- drug interactions between acid suppressive drugs and tyrosine-kinase inhibitors can be clinically relevant. The oral absorption of dasatinib, crizotinib, erlotinib, lapatinib, gefitinib and pazopanib can be substantially altered by concomitant use of acid suppressive treatment. If it is not necessary, the combination of these drugs with acid suppressive medications should be avoided.
Case report: 24-year-old woman was diagnosed with Philadelphia gene positive acute lymphoblastic leukemia nine years ago. The patient used acid suppressive drugs through her all treatments and continued using them. She treated with 8 courses of hyper-CVAD chemotherapy regimen and imatinib 600 mg/day and continued using imatinib for 2 years with bad compliance. After recurrence of patient's malignancy, imatinib was switched to dasatinib 140 mg per day. After some serious side effects, nilotinib was prescribed. But patient's genetic tests showed that bcr-abl mutation ratios were increasing therefore again dasatinib 100 mg per day therapy was started. With this treatment major molecular response had been achieved but bcr-abl positiveness was still an issue. After genetic tests revealed that patient's Philadelphia chromosome is 0.18 positive, haplo-allogenic bone marrow transplantation was planned from her brother. The interaction between dasatinib and lansoprazol is brought to physician's' attention and proton pump inhibitor therapy is changed to antacid supplements before 13 days of transplantation. Patient received antacid suspensions and sucralfate at least 2 hours before or after dasatinib administration instead of lansoprazole. Patient's pH chromosome test results started to become negative and transplantation was successfully performed. Her latest gene flow showed no positiveness of Philadelphia chromosome. Patient is fully recovered and accepted by clinicians in fully remission
Discussion: The usage of PPIS and H2RA is common and it may not be a good decision to prescribe those type medicines to patients that are on tyrosine-kinase inhibitor drug treatment
Conclusion: Altered bioavailability of tyrosine-kinase inhibitors due to acid suppressive therapy is an important issue. Therefore drug-drug interactions must be a prominent issue that is taken into account when planning patients' cancer therapy. Physicians and clinical pharmacists should be aware of these interactions and take necessary precautions.

PP-63

Recombination frequencies in HLA loci among Turkish patients with hematological malignancies and their family-based donors

Ç. Kekik Çınar[1], G. Karahan[2], A. Kaya[2], S. Kalayoğlu-Beşışık[3], F.S. Oguz[2]
[1]Istanbul Faculty of Medicine, Department of Medical Biology; [2]IU Istanbul Faculty of Medicine, Department of Medical Biology; [3]IU Istanbul Faculty of Medicine, Department of Hematology

Objective: Allogeneic hematopoietic stem cell transplantation (HSCT) is a treatment option with growing performance for leukemia, aplastic anemia and genetic disorders. The genes of MHC gene locus include DNA segments with high or rather low recombination frequencies. The frequency of recombination is increased at loci close to the telomeres and in female gender. The aim of the present study is to document the recombination events by pedigree diagrams with the primary goal to determine the frequency of recombination in a different ethnic population from mostly reported studies regarding European population.
Results: Altogether 8695 allogeneic HSCT recipients and their family based potential donors (n=34227) were included in this retrospective study. Recombinations were determined in 106 (F/M: 47/59) out of 8695 families enrolled into the study. These recombinations were present in 43 (40.6%) of the patients (range: 5–70 years, mean age 28.44±2.5; F/M: 20/23), and 63 (59.4%) of healthy donors (range: 11–68 years, mean age: 37.14±15.8; F/M: 27/36). The frequency of recombinations was 0.48% and 0.18%, in patients and donors, respectively. Of the 106 recombinations, 60 were detected in A locus (19 in patients), 5 in B locus (1 in patients) and 38 in DR locus (20 in patients).

Three of the 106 recombinations were observed in the C, DQ and DP loci, and all in the patient.

Conclusion: In our study, due to recombinations in HLA-A,-B or -DR loci, we found that some patient-donor pairs became 6/5 matched instead of 6/6 (n=42), eliminating the allogeneic HSCT possibility for the patients from the full-matched siblings. To our knowledge, this is the first study reporting the recombination frequencies in HLA loci among Turkish population and thus, providing informative data to the clinicians regarding the cross-over possibilities in Turkish patients with hematological malignancies.

PP-64

The impact of iron deficiency on blood cell volume

M. Yorguc, U. Kısa, E. Yorguc, M. Albayrak
Kırıkkale Unıversity Hospital

Objective: Iron is the one of the most important elements that has a role in DNA and RNA synthesis. Cell proliferation and differentiation are affected during hematopoiesis just because iron has a role in production of enzymes, like ribonucleotide reductase, which play a part in forming DNA, iron deficiency affects telomerase enzymes that maintain continuity of DNA sequence and also decreased levels of antioxidant enzymes are observed in iron deficiency.

Methodology: In our study, we observed the effect of iron deficiency in mean corpuscular volume, mean reticulocyte volume (MRV), mean lymphocyte volume (MLV), mean monocyte volume (MMV), mean neutrophil volume (MNV), mean eosinophil volume (MEV) and mean platelet volume (MPV). Patients who are 2–18 years old, have no signs of active infection and chronic disease; no history of iron treatment for last six months; and applied with the anemia. Patients with <12 ng/ml ferritin value are accepted as iron deficiency patients. 96 children with iron deficiency and 76 children who had not iron deficiency are included in the study.

Results: Consequently, iron deficiency results in both quantitative and qualitative changes in blood cells. It is interesting that decrease in MCV, MRV, MNV and MEV and increase in MLV, MMV and MPV are stated in our study.

Conclusion: We think that take into consideration of these parameters into clinical usage could decrease both investigation and health expenses for diagnose. Our study has different from other studies just because our study has higher number of cases and evaluated in childhood.

PP-65

Cardiac amyloidosis

S. Shabanova, V. Huseynov
Azerbaijan Medical University

Objective: Amyloidosis is a fatal disease of the light chains of immunoglobulins, which, being a multisystem disease, is accompanied by the deposition of amyloid fibrils in organs such as the kidneys, heart, lungs, digestive system. Unfortunately, in the case when amyloidosis (AL-A) is accompanied by damage to the heart, the prognosis is very poor. This case tells about a 55-year-old patient with arrhythmia, who has shortness of breath during physical movement.

Case report: Physical examination revealed leg edema, bruising of the skin around the eyes, increased blood pressure. ECG: supraventricular tachycardia, prolonged PR interval; Echo-KG: EF 50%, amyloid-like lesions in the myocardial tissues, a restrictive type of diastolic dysfunction, tricuspid insufficiency of a moderate degree, SPAP 75mmHg, with diastole revealed 8 mm of pericardial fluid. With cardiac MRI, amyloid changes are seen in the left ventricle. Indirectly marked violation of diastolic function. During examination we could not get a cardiac biopsy. Rectal biopsy for staining by Congo Red is positive. Haemogram: mild neutrophilic leukocytosis, normochromic anemia, increased erythrocyte sedimentation rate(ESR).Biochemical analyses: Ca 10.49 mg/dl, creatinine 0.6 mg/dI, IgA 0.28 g/l, IgG 8.06 g/l, IgM 0.35 g/l, total protein 7.23 g/dl, albumin 4.55 g/dl, CRP 5.88 mg/dl, LDH 220 U/L. In the bone marrow 9.8% of binucleate and triple nuclear plasma cells, during the urine immunofixation test the lambda type of the light chain was detected, the increase in the concentration of the light lambda chain was 3.24 (N 0–1.5) and the serum immunofixation test revealed bands characteristic of monoclonal gammopathy, the kappa/lambda ratio was 1.12. On the basis of instrumental and laboratory studies, the patient was diagnosed with cardiac amyloidosis.

Methodology: ECG: Echo-KG: Cardiac MRI, Rectal biopsy, Haemogram, Biochemical analyzes, Bone Marrow, Serum immunofixation

Results: The patient, based on the VRD protocol, was treated with chemicals. After 2 courses a decrease in amyloid lesion in the eye area was observed, 30–40% of regressions were observed on cardiac MRI. The patient is under the supervision of a cardiologist and a hematologist.

Conclusion: An autologous bone marrow transplantation is planned.

PP-66

Metabolic syndrome post allogeneic stem cell transplantation in adult patients is not an uncommon complication: a single-center experience

P. Kaloyannıdıs[1], D. Awamı[1], S. Kanfar[2], Z. Al Shamması[2], H. Raslanı[3], R. Attas[3], A. Dayel[3], H. Al Hashmı[2], K. Al Anezı[2]
[1]Adult Hematology & Stem Cell Transplantation Department, King Fahad Specialist Hospital, Dammam, Saudi Arabia; [2]Adult Hematology & Stem Cell Transplantation Department, King Fahad Specialist Hospital, Dammam,Saudi Arabia; [3]Pathology and Lab Medicine Department, King Fahad Specialist Hospital, Dammam,Saudi Arabia

Objective: Currently, the survival rates post allogeneic transplantation (alloHCT) have been significantly prolonged therefore, complications other than the Graft vs. Host disease (GvHD) or disease recurrence, have become increasingly important. The post-transplant metabolic syndrome (PT-MS), caused by several factors (i.e. immunosuppressive agents, chemo-radiotherapy, anti-viral, and biologic therapies) is a well-known post-transplant complication in pediatric allografted long-term survivors however, only a few studies have evaluated the prevalence of the PT-MS in adults. In this retrospective study, we sought to evaluate the incidence, risk factors and impact of the PT-MS on alloSCT outcome.

Methodology: From 1/2011 to 12/2018, 54 patients (34 males and 20 females) with adequate clinical and laboratory data and a minimum follow-up of 6 months were included in the study. Their median age was 35.6 (16–67) years and following a myeloablative (n=34) or reduced intensity (n=20) regimen patients received either a mobilized peripheral blood stem cell (n=45) or marrow (n=9) graft originating from full-matched siblings (n=46) or haploidentical (n=8) donors. Calcineurin inhibitors plus either short-term Methotrexate or Mycophenolate Mofetil were given as GvHD prophylaxis. Diagnosis of PT-MS was based on NCEP-ATPIII criteria; for patients with unknown data for abdominal circumference, a modified criterion of body mass index (BMI) ≥25 kg/m^2 was utilized instead. The independent t-test, logistic regression analysis and log-rank tests were used for statistical analysis.

Results: Twenty-four (44%) patients (14 males, 10 females) fulfilled the criteria for PT-MS. Twenty had been diagnosed after the 1st trimester, 3 patients after the 2nd and in addition 1 after the 3rd trimester post alloSCT. Twenty out of 24 (83%) patients had elevated glucose, 19/24 (80%) had BMI >25 kg/m^2, 18/24 (75%) elevated triglycerides levels, 14/24 (60%) low HDL levels and 13/24 (55%) hypertension. Six (25%) had a known history of MS before alloSCT (10 patients had no available data to assess for MS diagnosis prior to alloSCT). Interestingly, in 8/24 (33%) patients who had PT-MS diagnosed early, either in the 1st or 2nd trimester, the syndrome was completely reversible beyond the 6-month post alloSCT follow-up period. In the aforementioned statistical models, patients\' gender, age, BMI, type of conditioning regimen and GvHD co-existence were evaluated as potential predisposing factors for the PT-MS. In univariate and multivariate analysis only BMI >25 kg/m^2 and age >35 years were detected as significant risk factors ($p<0.01$) for development of PT-MS. The PT-MS did not adversely impact survival or the NRM incidence post alloSCT.

Conclusion: In our study, in agreement with other publications, we demonstrate that the PT-MS is not an uncommon complication in the early post-transplant period however, for approximately 1/3 of patients the syndrome was reversible. For patients with high risk features (BMI >25 kg/m^2, age >35 years, known history of diabetes-mellitus, dyslipidemia,

hypertension) apart of close monitoring, specific diet and encouragement for exercise might help reduce the incidence and severity of PT-MS. Nevertheless, prospective and well design trials are warranted to determine the incidence, severity and impact of PT-MS on alloSCT outcome for adult patients.

PP-67

Late renal aspergilloma after autologous stem cell transplantion mimicking secondary malignancy

M. Altınkaynak[1], S. Kalayoglu Besisik[2], C. Tascioglu[1]
[1]İstanbul University, İstanbul Medical Faculty, Department of Internal Medicine, Istanbul; [2]İstanbul University, İstanbul Medical Faculty, Department of Internal Medicine Hematology, Istanbul

Background: Aspergillosis limited to the urinary tract is a rare disease, often occurring in immunocompromised patients. Aspergillus fumigatus was the most common isolate. Three different patterns of renal Aspergillus infection have been described: disseminated aspergillosis with hematogenous renal involvement, aspergillosis of the renal pelvis with bezoars formation, and ascending panurothelial aspergillosis. Renal involvement is usually silent if the disease is localised to the cortex of the kidney and is a relatively frequent finding at autopsy in the context of disseminated disease. The typical host group is the leukaemic, organ and stem cell transplant (SCT) patient. We describe a case of renal aspergillosis with mass formation in a 54 years old male lymphoma patient who presented with hypercalcemia, renal failure and severe malaise.

Case report: A 54-year-old man presented with nausea, vomiting, and severe weight loss. Twelve years before, he had been diagnosed with follicular lymphoma for which he had received CHOP chemotherapy and undergone autologous SCT. He had a history of fungal infection in the nasal sinuses and lungs and hypogammaglobulinemia since transplantation to date. Upon presentation to our hospital, he was afebrile. A thoracic CT showed extensive bilateral cavitary lesions with the largest reaching 5.7 cm in diameter. Laboratory values were showing acute kidney failure with a creatinine of 2.2 mg/dL. He had hypercalcemia of 11.5 mg/dL with normal serum 25(OH)2D level. Intact serum parathyroid hormone (PTH) was decreased. PTHrp and serum 1,25(OH)2D levels could not be analyzed due to technical failure. He denied taking any calcium and vitamin D including agent. Serum CRP and ESR were remarkable elevated. He had mild normocytic anemia. Intravenous normal saline was initiated. Abdominal CT demonstrated a smooth contoured mass lesion in the inferior pole of the left kidney, which was iso-hypodense to renal parenchyma and showed exophytic extension sized 3.4×3.1 cm. The patient was long time in hematologic remission. Secondary malignancy was suspected with pulmonary infection which would be related with either mycobacterium or fungal infection. Broncoscopic evaluation did not reveal any mycobacterium infection laboratory data. An ultrasonography-guided fine needle aspiration was carried out from the mass in the left kidney. The pathology finding was compatible with a renal aspergilloma. For anti-fungal treatment liposomal amphotericin B was administrated with a dose 5 mg/kg/day. In 2 months the patient recovered well as improvement in calcium and acute phase reaction.

Conclusion: In conclusion, renal aspergilloma should be remembered in the differential diagnosis of renal masses detected by radiological imaging modalities in patients with conditions predisposing them to aspergillosis. For a definitive diagnosis and treatment plan, it is recommended imaging-guided sampling from suitable lesions, followed by histopathological and/or microbiological examination. Coincident hypercalcemia is well described in various granulomatous disorders. Among fungal diseases, disseminated candidiasis, histoplasmosis, cryptococcosis and coccidioidomycosis have rarely been implicated as causes of hypercalcemia. The responsible factor may be 1,25(OH)2D. Total serum levels of 1,25(OH)2D may not be elevated, but inappropriately high for the circumstances. Free 1,25(OH)2D levels should be determined in this situation

PP-68

Clinical implications of the methylenetetrahydrofolate reductase (MTHFR) C677T gene polymorphism on outcomes of allogeneic hematopoietic stem cell transplantation: systemic literature review

M. Mohammed Saleh
King Faisal Specialist Hospital and Research Center, Riyadh, SA; Clinical Hematology Unit, Internal Medicine Department, Assiut University Hospital, Assiut, Egypt

Objective: Inter-individual genomic variation, including pharmacogenes, could provide explanation for observed variability in the occurrence of complications following hematopoietic stem cell transplantation (HSCT) as graft versus host disease(GVHD), sinusoidal obstruction syndrome (SOS), oral mucositis (OM), drug induced hepatic and renal adverse events. Methylenetetrahydrofolate reductase (MTHFR) catalyzes the irreversible conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate and directs the flux of intracellular folate toward the conversion of homocysteine to methionine at the expense of nucleotide synthesis. A common genetic polymorphism, C677T, has been described for this enzyme; results in amino acid changes, at codons 222. The homozygous 677TT genotype, which occurs in approximately 10% to 15% of Caucasian and Asian populations, has been shown to have 30% of the MTHFR wild-type enzyme activity in vitro, and the heterozygous (CT) genotype has approximately 60% of wild-type enzyme activity.

Methodology: Herein, systemic literature review about impact of MTHFR C677T on clinical outcomes of HSCT. A Medline (PubMed), google scholar and Cochrane Database of Systematic Reviews search using key words "MTHFR C677T and HSCT", "pharmacogenetics and HSCT", "drug metabolizing enzyme gene polymorphism and HSCT" was undertaken in June 2019.

Results: 18 publications had been identified, all in retrospective fashion. Seven studies tested both patients' and donors' genomes for analysis with outcomes. One group studied 3 different HSCT outcomes in 3 different publications. Another group tested C677T with and without folinic acid rescue post HSCT for the same cohort in 2 different publications. Among 7 studies analysed OM as HSCT outcome, two studies showed higher incidence or greater OM with variant genotypes. Two studies reported slow PLT recovery post HSCT, another one showed trend for delayed neutrophil engraftment with variant genotypes. Conflicting conclusions had been reported regarding AGVHD, 3 studies showed the variant CT, TT genotypes to be associated with lower incidence of AGVHD, while another 2 studies reported higher incidence of AGVHD with those variant genotypes; with higher liver AGVHD in Asian population noted. Nonuse of folinic acid was associated with early and severe AGVHD with both patients' and donors' wild genotype 677CC in one study. Donors' variant genotype was significantly associated with higher risk of AGVHD and death in one study. Higher hepatic toxicity in relation to the variant genotype in one study from Korea, while no such relation found in another 7 different studies; one of them studied liver toxicity as lone outcome in patient received busulfan/cyclophosphamide as conditioning. No association to SOS had been reported in any study. Higher TRM with 67TT genotypes was reported in Korean population in 2 publications. Poor OS noted in relation to the variant genotype in 3 studies; 2 with patient genome and the third with donors. There were six studies with total of 488 patients negative for any association with C677T polymorphism

Conclusion: Variant MTHFR C677T genotypes associated with high liver toxicity in Asian populations received HSCT. Genotyping for MTHFR C677T before HSCT could have clinical significance. Randomized prospective studies are warranted to identify such potential pharmacogenetic marker with sufficiently strong evidence to be used in clinical practice.

PP-69

Successful treatment with azacytidine for simultaneous occurrence of acute myelomonocytic leukemia and multiple myeloma

Ü. Ataş[1], G. Tazegul[1], O. Yücel[1], T. Ulaş[2], O. Salim[1], L. Ündar[1]
[1]Akdeniz University Faculty of Medicine, Department of Hematology; [2]Near East University Faculty of Medicine, Department of Hematology

Background: Simultaneous occurrence of MM and AML is rarely described previously. In this case, we report an elderly patient with simultaneous MM with AML successfully treated with azacytidine for 15 months.
Case report: A 71-year-old male patient was referred to our clinic with immune paresis and IgG-Lambda monoclonal antibody. He had arthralgias and fatigue for several months. He was otherwise healthy. Physical examination was unremarkable. Blood counts at the time were hemoglobin 9.7 g/dl; platelets, 154×10^9/l; WBC, 2.3×10^9/l; neuthrophil, 0.7×10^9/l; monocytes 0.08×10^9/l; creatinine; 0.6 mg/dL and calcium; 9.1 mg/dL. MRI imaging of spinal vertrebrae showed several lytic lesions in cervical vertebrae. Flow cytometry and bone marrow smear showed an atypical monoclonal plasma cell proliferation. Patient was diagnosed with MM and received 1st cycle of weekly bortezomib-cyclophosphamide-dexamethasone (VCD); he was subsequently admitted with pneumosepsis several weeks later. During his follow-up in intensive care, immune paresis was resolved, however, blood counts were hemoglobin 10.1 g/dl; platelets, 173×10^9/l; WBC, 35.6×10^9/l; neutrophil, 9.7×10^9/l; monocytes 0.57×10^9/l and monoblasts were seen on peripheral blood smear. Both myelomonoblasts and atypical plasma cells were seen in a repeat blood marrow smear. A review of previous flow cytometry showed that a myelomonocytic blastic component was present to a lesser extent as well. During this process, bone marrow biopsy results were reported as Lambda monoclonal proliferation of 10–20% with myeloid maturation arrest. Patient was diagnosed as AML and MM, azacytidine monotherapy was induced, both MM and AML clones responded well to treatment and patient was clinically stable for 15 cycles. However, after 15 cycles, he was admitted with an episode of pneumosepsis, both MM and AML clone lost response to therapy, and patient succumbed to septic shock.
Conclusion: Plasmacytosis is known to occur in acute myeloid leukemia (AML), plasma cell count can increase post-treatment, in certain cases, to levels that may simulate multiple myeloma (MM). A few previous cases of pronounced plasmacytosis at the time of diagnosis of AML have been described in literature. Most cases described had leukemia occurred secondary to therapy. The present case posed a diagnostic challenge since the patient was firstly diagnosed as MM only, and AML clone was only more pronounced after the first VCD cycle. We hypothesized that the proliferation of myeloid immature clone may be increased by immunosuppression after the initial VCD treatment protocol. Furthermore, we based our treatment strategy over AML, because of we thought that AML will be the main determinant of overall survival rather than multiple myeloma. On the other hand, treatment options for elderly AML are limited. Since hypomethylating agents used in AML were also reported to be effective on plasma cells, azacytidine monotherapy was chosen as treatment. In conclusion, we report a patient diagnosed with simultaneous AML and MM successfully treated with azacytidine. This regime could be a reasonable option for future cases with similar diagnosis. In our case, azacytidine was effective for both AML and MM for 15 months.

PP-70

The beneficial effects of varicella zoster virus

K. Al-Anazi[1], W. Al-Anazi[2], A. Al-Jasser[3]
[1]King Fahad Specialist Hospital; [2]King Fahasd Specialist Hospital; [3]Genaral Health Directorate in Riyadh

Background: Varicella zoster virus (VZV), a highly contagious double-stranded DNA virus that belongs to the alpha group of herpes viruses, causes chickenpox in childhood and herpes zoster (HZ) in adults. VZV behaves differently from other herpes viruses and it has the following characteristic features: having the smallest viral genome, losing almost all the genes that are not essential for its survival, being cell-associated and highly fusogenic, lacking inhibitors of autophagy, being an exclusively human pathogen, having a species-specific cytokine profile, and having an inverse relationship with glioma.
Results: The recently reported beneficial effects of the virus that have translated into prolongation of survival include: (1) stimulation of bone marrow (BM) activity in patients with hematologic malignancies (HMs) and BM failure syndromes, (2) antitumor effects in various HMs and solid tumors, and (3) association with graft versus host disease which has anticancer effects. Examples of the reported beneficial effects of VZV infections include: (a) in a single center, retrospective study that included 16 episodes of VZV infections occurring in 14 patients with various types of HMs and BM failure syndromes, Al-Anazi et al. (Eur J Haematol, 2005) reported an increase in white blood cell count, hemoglobin (Hb) level, and platelet count starting approximately 6 weeks following VZV infections and this stimulation of the 3 hematopoietic cell lines in the BM that followed VZV infections was maintained for more than 3 years following the infection; (b) in a retrospective study that included a large number of patients with multiple myeloma subjected to high-dose melphalan followed by autologous hematopoietic stem cell transplantation (HSCT) after control of their primary disease, Kamber et al. (Bone Marrow Transplant, 2015) reported that approximately one third of these patients developed VZV infections either before or after HSCT and that despite encountering VZV infections in patients with worse expected prognosis, the OS in patients who developed VZV infection was superior to that in patients who never developed the infection; and (c) Al-Anazi et al. (J Hematol Clin Res, 2019) reported a BM biopsy-proven reversal of pure red cell aplasia manifested by a gradual increase in Hb level starting 6 weeks following a localized HZ infection till the Hb level plateaued above 14 g/dL fourteen months following HZ. Additionally, there are several reports on the safety of the live-attenuated even in severely immune suppressed individuals and emerging role of VZV in cancer immunotherapy.
Conclusion: The reported beneficial effects may occur through several immunological mechanisms including: alterations in BM microenvironment; cells involved in the pathogenesis of the virus such as: mesenchymal stem cells, dendritic cells, and natural killer cells; cellular proteins such as open reading frames, glycoproteins, promyelocytic leukemia protein, chaperons, and small ubiquitin-like modifier proteins; extracellular vesicles, exosomes, and micro-RNAs; as well as signaling pathways, cytokines, chemokines, and interferons. Ultimately, the virus itself; modified or engineered versions of the virus; or specific elements obtained from the serum of patients infected with VZV may become novel therapeutic modalities in the management of patients with BM failure, HMs and solid tumors.

PP-71

Gemtuzumab ozogamicin in the treatment of critically ill patients with refractory acute myeloid leukemia

D. Zaytsev, L. Girshova, V. Ivanov, I. Budaeva, D. Motorin, R. Badaev, K. Bogdanov, J. Mirolubova, T. Nikulina, T. Chitanava, J. Alexeeva, A. Zaritskey
Federal Almazov National Medical Research Centre

Objective: Patients with refractory acute myeloid leukemia (AML) are often critically ill. Acute infections leading to sepsis as well as to extramedullary lesions with an organ dysfunction mainly contribute to a critically ill status. Nowadays, data about successful using of anti-CD33 gemtuzumab ozogamicin (GO) have been reported. The efficacy of GO could probably arise not only from blast clearance and also due to its immunomodulatory effects.
Methodology: We had three patients with primary refractory AML, who were critically ill at the time of a therapy initiation. All the patients had high blood and bone marrow blast percentage, symptoms of systemic inflammation, high recurrent fever, high CRP level and increased level of hepatic enzymes, two patients had lung disorders with massive pulmonary infiltrates, one of those patients experienced respiratory failure, one patient had acute kidney damage. They have been treated by the combination of gemtuzumab ozogamicin (3 mg/m^2) with azacitidine (75 mg/m^2 days 1–7). This drug combination led to a rapid organs function normalization during a week after the therapy initiation, an apyrexia achievement on the first-second day with a decreasing of systemic inflammatory response indicators during the first days of the therapy. Acute kidney damage entirely resolved during the first

two week of the therapy. In the case of patients with lung disorders, blood gas normalization was noticed on the first day as well. CT scan revealed a significant regression of pulmonary infiltrates in the size on day three with a further reduction infiltrates in a dynamic observation. It is important to note, that antimicrobial/antifungal therapy was not changed during the described period.

Results: We observed very rapid effects in three critically ill patients with refractory AML on GO therapy: blasts reduction in blood (after a few days of the therapy) and marrow (on the days 3–16 of the therapy), rapid organs function and blood gas normalization on day one-two, an apyrexia achievement on the first-second day, resolution of respiratory and kidney failure and significant reduction of pulmonary infiltrates on CT scan on day three.

Conclusion: We suppose, that the therapy by GO in the combination with azacitidine, finally, have led to a critically ill state resolution and discharge of the patients from ICU.

PP-72

A case of thrombotic thrombocytopenic purpura related to brucellosis

S. Balta[1], F. Uslu[1], O. Ekinci[2], M. Merter[2]
[1]Fırat University Faculty of Medicine Internal Medicine Department; [2]Fırat University Faculty of Medicine Hematology Department

Background: Thrombotic thrombocytopenic purpura (TTP) is a syndrome of microangiopathic hemolytic anemia (MAHA) and characterized by the pentad of negative hemolytic anemia, fever, renal abnormalities and neurological disturbances. There are several causes for TTP. But there are only a few case reports that identify brucellosis as a potential cause of TTP. Here we report our TTP case with concomitant brucellosis.

Case report: A 51-year-old male patient presented with fever, thrombocytopenia, renal failure and somnolence. Patient's past medical history was unremarkable. At presentation, his creatinine level was 1.74 mg/dL, hemoglobin level was 9 g/dL, platelet count was 16,000/μL, lactate dehydrogenase level was 910 u/L, indirect bilirubin was 1.2 mg/dL and direct coombs test was negative. Coagulation tests were normal. In peripheral smear evaluation, there were 12–13 schistocytes per high power field. ADAMTS-13 antigen was <0.01 IU/mL. Daily plasma exchange was started immediately. At day 9 platelet count was recovered. Additional two courses of plasma exchange was performed. For the etiology, a full body computed tomography performed after renal functions was normalized and it was normal. Rheumatologic tests were negative. Brucella agglutination test was positive at a titer of 1/320. Antibiotic treatment was started for brucellosis. After 4 months no recurrence was observed.

Conclusion: There were several etiologic factors that defined for TTP. But when it comes to brucellosis there were only seven case reports in literature that associates brucellosis with TTP. Ours was the eighth. All cases in literature was recovered with plasma exchange and antibiotics. With all these case reports suggest that brucellosis can be an etiological factor for TTP and it must be kept in mind in endemic regions.

PP-73

Discontinuation of tyrosine kinase inhibitors in chronic myeloid leukemia: a single-center experience

R. Frikha[1], M. Elloumi[2], H. Kamoun[1]
[1]Department of Medical Genetics; [2]Department of Hematology

Objective: BCR-ABL1 tyrosine kinase inhibitors (TKIs) have dramatically transformed the treatment of patients with chronic myelogenous leukemia (CML). Currently; several clinical trials have demonstrated that some patients with chronic myeloid leukemia in chronic phase (CML-CP) who achieve sustained deep molecular responses on tyrosine kinase inhibitor (TKI) therapy can safely suspend therapy and attempt treatment-free remission (TFR). The aim of this study was to assess discontinuation of tyrosine kinase inhibitor (TKI) treatment in Tunisian patients with chronic myeloid leukemia (CML).

Methodology: 12 Tunisian CML patients who discontinued TKIs were followed. Quantitative assessment of the BCR-ABL transcript was performed using the Cepheid Xpert BCR-ABL ultra assay. Duration of TKI therapy, depth of molecular response and the reasons for TKI discontinuation were collected.

Results: The median duration of TKI therapy was 10 years (range 2–14). The reasons for discontinuation were as follow; durable and deep molecular response (9 cases); pregnancy (2 cases) and adverse effect of therapy (1 case). The median follow-up after TKI therapy discontinuation was 7 months (1 to 44 months). Relapses occurred after a median time of 5 months (range: 1–21). 5 patients (42%) experienced a molecular relapse defined as the loss of a major molecular response (MMR).

Conclusion: Despite the limit of our study, these results emphasize the importance of sustained DMR for TFR duration.

PP-74

A clinical analysis of 15 cases of coexistence of T-cell and B-cell lymphoma: a retrospective study of the Polish Lymphoma Research Group

S. Bartyzel[1], D. Zımowska-Curyło[1], M. SokołOwska-Wojdyło[2], M. Wıtkowska[3], E. Chmıelowska[4], J. Romejko-Jarosıńska[5], J. Drozd-Sokołowska[6], A. Gıza[1]
[1]Department of Hematology Jagiellonian University, Krakow, Poland; [2]Department of Dermatology, Venerology and Allergology, Medical University of Gdansk, Gdansk, Poland; [3]Department of Experimental Hematology, Medical University of Lodz, Lodz, Poland; [4]Department of Oncology, NU-MED, Tomaszów Mazowiecki, Poland; [5]Department of Lymphoid Malignancies, Maria Sklodowska-Curie Institute and Oncology Center, Warsaw, Poland; [6]Department of Hematology, Warsaw University, Poland

Objective: The coexistence of CTCL and B lymphocyte malignancy in the same patient is rare. Most of the available descriptions are isolated case series. There are several hypotheses trying to explain this coexistence: a common origin of both malignancies from neoplastic stem cell, a coincidence of two unrelated neoplasms, exposure to carcinogens or viruses, radiation and previous cytostatic treatment. Some data also indicate that patients with mycosis fungoides (MF) are at increased risk of development of secondary malignancy – including lymphoma.

Methodology: The retrospective study from 6 Polish haemato-oncology centers on a group of 15 patients - 8 male pts (53.3%), 7 female pts (46.6%) aging 58–88 (average 69.6) with coexistence of CTCL and B cell malignancy was conducted. According to the family and previous medical history, the onset of both malignancies, the course of the diseases, methods of treatment and outcomes specified by survival rate and assessment of clinical remission were evaluated.

Results: In 10 of reported 15 cases family history was negative for malignancy, for remaining 5 pts data were not available. Types of diagnosed B cell lymphoma included HL (6 pts), DLBCL (7 pts) and CLL (3 pts), whereas for T cell lymphoma – MF (12 pts) and cALCL (3 pts). In 5 pts (33.3%) other cancers (3 breast cancers, 1 kidney and 1 prostate cancer) before occurrence of B or T cell lymphoma were diagnosed – the average time from solid tumor diagnosis to the onset of lymphoma was 9.4 years. All 3 cases of pts with breast cancers history developed DLBCL later. In 4 of 5 cases of previously diagnosed tumor T cell lymphoma developed after diagnosis of B cell lymphoma. Additionally, 2 of those 5 cases were diagnosed with two types of B cell lymphoma (CLL and HL; CLL and DLBCL). In 7 pts B cell lymphoma was diagnosed as first malignancy, in 6 pts - T cell lymphoma, in 2 pts it was simultaneous diagnosis. Furthermore, in both cases of simultaneous diagnosis, treatment with interferon alpha for MF preceded development of DLBCL (in average time of six months). In 6 cases of pts with earlier diagnosis of T cell lymphoma, 3 of them had recurrence after treatment of B-cell lymphoma later and 1 pt had only partial remission of disease. We observed also coexistence of HL and MF in 5 cases. At the time of this presentation 3 of reported 15 patients were deceased (1 case of lung tumor, 1 case of ileus, 1 case unknown).

Conclusion: In our report the coexistence of HL and MF is not as rare as in previous studies. In contrast to other studies our analysis suggests that there is no difference between the order of T-cell or B-cell lymphoma occurrence. The frequency of overlapping of different types of malignancy is high which points to complex and probably common genetic background and impaired immune anti-cancer response.

PP-75

Lack of association between MTHFR C677T and risk of chronic myeloid leukemia

M. Ben Jemaa[1], F. Turki[2], H. Kamoun[2], R. Frikha[2]
[1]Faculty of Medicine; [2]Department of Medical Genetics

Objective: Methylenetetrahydrofolate reductase (MTHFR), a critical enzyme in folate metabolism is involved in DNA methylation and nucleotide synthesis. The common MTHFR single nucleotide polymorphism C677T has been reported to be associated with various cancer. The aim of this study was to investigate the influence of the 677 C>T polymorphism in the MTHFR gene on the risk of developing chronic myeloid leukemia (CML).
Methodology: We performed a case-control study in a Tunisian population of 20 patients with CML and 35 healthy control subjects. MTHFR C677T polymorphism genotyping was assessed using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method.
Results: The results demonstrated no statistical difference in MTHFR 677 frequency distribution between patient and control groups.
Conclusion: Our findings suggest that MTHFR 677 gene variants have no influence on the susceptibility to CML in a Tunisian population.

PP-76

MRD as an optimal treatment outcome assessment tool

M. Shervashidze, A. Popa, N. Batmanova, G. Mentkevich
N. N. Blokhin NMRCO

Background: At the present time, very good survival in children with ALL has been achieved. However, there is a group of patients who develop a relapse of the cause of the disease, which is not fully understood. That is why the search for new optimal indicators for monitoring the state of tumor cells. According to many research MRD is one of the important elements of the response to treatment, and may be the basis for the correction of therapy.
Aim: The aim of our study evaluates the significance of MRD as a basic tool of stratification and the impact of the level of the MRD on the overall survival (OS), event-free survival (EFS) and disease- free survival (DFS).
Methodology: from 2010 to 2017 ninety-one pediatric patients with B ALL were enrolled in ALL IC BFM 2009. Median age 5.2 years (range from 1–16). Male 37, female 54. The diagnosis was made by standard morphological analysis and by flow cytometry immunophenotyping. 81 patients had common ALL, 4 pre-B ALL, 6 pro-B ALL. Initial risk group definition Based on age, leukocytosis, genetic translocation. Accordingly, in standard risk group included 24 patients (SR), twenty-eight in the intermedia risk group (IR) and 4 high risk (HR). Assessment of MRD was carried out on 15 days of induction therapy. Our studies used 4- and 8-color flow cytometry.
Results: Level MRD <0.1% detected on 41 (46.1%) patients, MRD between 0.1 and 10% had 38 (42.7%) patients and MRD ≥10% had 10 (11.2%). Morphology seventy patient had <5% (M1) blast BM, 15 patients had from 5 to 25% (M2) and 5 patients ≤25% blasts. Based on the level of MOB eight patients from the standard risk group were transferred to intermediate risk group, and 8 patients from intermediate to high risk group. 5y-EFS MRD <0.1% 85.9±7.8%, for MRD from 0.1 to 10% 83.1±7.1%, MRD ≥10% 78.8±13.4% (p=0.2) Stratification by the ALL-BFM 2009 risk criteria on 15d resulted in 5y-EFS of 100% (n=20) for SR, 80.3±7.1%(n=54) for IR, and 76.0±1.23% (n=16) for HR p=0.16. Given this stratification 5y-DFS was 100% (n=20) for SR, 80.9±7% (n=54) for IR, and 84.4±10% (n=16) for HR. Due to stratification based on MRD we were able to identify a group of "really" standard risk, survival which reached 100 percent. All re-stratification patients (changed risk groups due to exclusively the level of MRD) achieved complete remission and live without relapse.
Conclusion: Finally, our results confirm the importance of MRD analysis for risk adapted treatment childhood B ALL to use this to determine the intensity of postinduction therapy. Based on the results of the study entry, we can conclude that the use of MI as the main tool of the risk of adapted therapy has made it possible to achieve an improvement in survival for patients of the standard risk group.

PP-77

Acute liver failure secondary to dacarbazine use in a Hodgkin lymphoma patient

T. Cetıntepe[1], S. Solmaz[1], D. Kıper[1], S. Tekel[2], B. Payzın[1]
[1]İzmir Katip Celebi University, Ataturk Training And Research Hospital, Department of Hematology; [2]İzmir Katip Celebi University, Ataturk Training and Research Hospital, Department of Internal Medicine

Introduction: Current standard treatment of Hodgkin lymphoma (HL) is expected to cure the majority of patients, but treatment related toxicities have become a competing cause of mortality. Dacarbazine is an alkylating agent used in the therapy of HL and associated with serum enzyme elevations during therapy. In this report, a liver failure associated with dacarbazine is presented.
Case report: Twenty-year-old man, admitted with weakness and swelling in the right axillary region. The patient's symptoms were accompanied by a prolonged fever, and weight loss. Right axillary lymph node biopsy revealed mixed cellularity classical HL with multiple Reed Sternberg and Hodgkin cells with immunohistochemical expression of CD30 and CD15. Bone marrow infiltration was observed. Laboratory test was reported as; hemoglobin 9 g/dl, leucocyte 3.1×10^3/µl, platelet 138×10^3/µl, ALT 31 U/L, AST 32 U/L, ALP 51 U/L, GGT 30 U/L, LDH 274 U/L, creatinine 0.6 mg/dl. Viral hepatitis markers, HIV and EBV serology were negative. Computer tomography (CT) scan showed cervical, mediastinal and retroperitoneal enlarged lymph glands, without liver lesions The patient clinically appeared to have stage IV-B mixed cellularity classical HL and received ABVD (doxorubicin 25 mg/m^2, bleomycin 10 mg/m^2 vinblastine 6 mg/m^2, dacarbazine 375 mg/m^2) protocol. Ten days after the administration of chemotherapy, patient admitted with weakness, jaundice and fever. Liver tests were noted to be abnormal: AST 46 IU/L, ALT: 67 IU/L. Five days later AST and ALT has risen to 4,202 IU/L and 1,995 IU/L, and Serum biochemistry showed LDH >1,995 U/L, total bilirubin; 8.3 mg/dl, direct bilirubin; 4.5 mg/dl, ALP 173 U/L, GGT 222 U/L, Albumin 3 g/dl. International normalized ratio (INR) was 2.27. Repeated serology for HIV and hepatitis B, C, CMV and EBV were negative. Blood and urine cultures were negative. Abdominal ultrasound was unremarkable. Computer tomography shows diffuse hypodensity observed in periportal tracts consistent with newly developed edema in liver. No evidence of thrombosis was detected by imaging methods. N-acetylcysteine infusion, ursodeoxycholic acid was started and hydration provided. Liver biopsy was not performed considering the general condition of the patient. On the fifth day, aminotransferases tended to improve, but bilirubin and INR continued to rise. Chemotherapy was delayed for one month, dacarbazine discontinued due to liver toxicity. AntiCD30 monoclonal antibody brentuximab was added to doxorubicin, bleomycin, vinblastine therapy. The patient is followed up with normal blood values at the third month of treatment.
Discussion: ABVD has been standard therapy for advanced HL. It is generally considered as safe and rarely has been reported to cause acute liver failure. We present an unusual case of liver toxicity due to dacarbazine therapy.
Conclusion: Although the side effects of many chemotherapy drugs are rare, detailed evaluations should be made in the patients control applications.

PP-78

Extranodal marginal zone lymphoma with orbital involvement: a case report

A. Tekinalp, S. Demircioğlu, S. Yılmaz, Ö. Çeneli
Necmettin Erbakan Univercity Meram Medical Faculty, Department of Internal Medicine Division of Hematology, Konya, Turkey

Introduction: Extranodal marginal zone lymphoma (MZL) of mucosa-associated lymphoid tissue (MALT) is a type of B-cell non-Hodgkin's lymphomas (NHL) and occurs for 7% of NHL. It has an indolent and heterogeneous clinically characteristic. Gastrointestinal tractus especially gastric involvement is seen common. However, MZL can involve salivary gland, lung, small intestine, skin or other soft tissues. In this poster we present a case with orbital involvement of MZL.

Case report: Sixty-four-year-old female patient; she consulted us with a right orbital mass lesion which had identified as marginal zone lymphoma by excisional biopsy. On examination, there was no pathological finding except of operation scar at right orbit. Complete blood count and biochemical parameters were normal as Hb 13.0 g/dL, WBC 7,000/µL, PLT 366,000/µL, urea 32.7 mg/dL, creatinine 0.76 mg/dL, uric acid 4.2 mg/dL, Na 137 mEq/L, K 4.5 mEq/L, Ca 10 mg/dL, LDH 220 U/L, AST/ALT 21/29 U/L, total bilirubin 1 mg/dL, direct bilirubin 0.4 mg/dL, GGT 22 U/L, CRP 0.1 mg/L. Viral serology was no abnormal also. She had no history of B symptoms. In PET/CT imaging we found cervical, mediastinal, hilar, paratracheal and carinal lymph nodes which were accepted reactive characteristic due to low FDG uptake. Involvement of bone marrow was not determined by biopsy. 180 cGy with 17 fractions radiotherapy (RT) was received. At 6th months after completed RT, newly developed cervical nodes, increased FDG uptake in older cervical and mediastinal nodes, newly developed intraabdominal and bilateral inguinal nodes with the largest diameter of 8×24 mm were detected by PET/CT imaging. Excisional biopsy from the newly inguinal lymph node was marginal zone lymphoma too. She then had rituximab (375 mg/m^2) plus bendamustin (90 mg/m^2) regime every four weeks for 4 cycles. In interim analysis after 4 cycles of chemotherapy, she had partial response. She has received fifth cycles of chemotherapy yet.

Discussion: Extranodal marginal zone lymphoma (MZL) of mucosa-associated lymphoid tissue (MALT) is most commonly seen in stomach and associated with Helicobacter pylori infection. However, an association between ocular adnexal lymphomas as our patient and Chlamydia psittaci infection was described. In addition to other some causative factors such as autoimmune disorders (SLE, Sjögren's syndrome), campylobacter and borrelia infections are related with MZL by stimulating immune processes. In our patient, serologic tests investigated for etiology were normal. Treatment of non-gastric MZL depends on stage of lymphoma and region of involvement. Regional radiotherapy as we preferred for first-line treatment and surgery may be useful in patients with local involvement. In advanced stages, this local treatment approach might not be enough to long-term control of disease. Single agent rituximab or rituximab plus chemotherapy such as CHOP, CVP, bendamustin may be preferred as initial treatment in patients with advanced stages, relapse or refractory disease also.

References

[1] Khalil MO, Morton LM, Devesa SS, et al. Incidence of marginal zone lymphoma in the United States, 2001-2009 with a focus on primary anatomic site. Br J Haematol 2014;165:67.

[2] Zucca E, Conconi A, Pedrinis E, et al. Nongastric marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue. Blood 2003;101:2489–95.

PP-79

A rare cause of hemophagocytic lymphohistiocytosis Q fever: a case report

B. Sağlam[1], M. Albayrak[1], A. Acar[2], A. Yıldız[1], S. Maral[1], M. Tığlıoğlu[1], İ. Battal[2], E. Şahin[3], A. Kuş[4]

[1]University of Health Sciences, Diskapi Yildirim Beyazit Training and Research Hospital, Department of Hematology, Ankara, Turkey; [2]University of Health Sciences, Diskapi Yildirim Beyazit Training and Research Hospital, Department of Infectious Disease and Clinical Microbiology, Ankara, Turkey; [3]University of Health Sciences, Diskapi Yildirim Beyazit Training and Research Hospital, Department of pathology, Ankara, Turkey; [4]University of Health Sciences, Diskapi Yildirim Beyazit Training and Research Hospital, Department of internal medicine, Ankara, Turkey

Objective: Hemophagocytic lymphohistiocytosis (HLH) is a rare disease with life-threatening increased inflammatory activity. The main symptoms of HLH are fever, hepatomegaly, splenomegaly and cytopenias. First described in 1952, this disease can be observed as family or secondary. Infections have an important place in secondary causes; HLH due to coxiella burnetti infection is very rare. Q fever is common in the world. Clinic of the disease; asymptomatic seroconversion, flu-like syndrome, pneumonia, hepatitis or chronic endocarditis. We aimed to present our case with high fever, pancytopenia and increased transaminase levels and a diagnosis of HLH secondary to Q fever.

Case report: A 28-year-old shepherd male patient with no known chronic disease or history of drug use admitted to our hospital with complaints of fatigue and high fever lasting for 1 week. On physical examination, liver and spleen were enlarged and fever was 38.6°C. Pancytopenia (Wbc 800/µL, Neu 200 µL, Hb 4.6 g/dl, platelet 10,000µ/L) and transaminase (AST 331 U/L, ALT 42 U/L) elevation was detected in the laboratory evaluation of the patient. The widespread in Turkey and preliminary diagnosis of CCHF was assessed by primarily because of the patient's profession. CCHF was not detected in the examinations and blood and urine cultures did not grow. Viral serology tests were negative except for coxiella burnetti phase I IgG 1/64 +. Biochemical tests showed high ferritin and hypertriglyceridemia. Therefore, the patient underwent bone marrow aspiration and biopsy with a preliminary diagnosis of HLH. Hemophagocytic cells were observed in bone marrow biopsy. The diagnosis of Q fever was confirmed after the patient was positive for coxiella burnetti phase II IgG 1/256 titer. According to HLH 2004 study, the patient who met 5 of the diagnostic criteria was diagnosed with HLH secondary to Q fever. After the first week of treatment, her fever completely decreased. In the second week, doxycycline treatment was completed and discontinued. After 8 weeks of treatment, his cytopenia and transaminases regressed and returned to normal. The patient is still under follow-up.

Conclusion: In patients presenting with pancytopenia and high fever, HLH should always be kept in mind because of its high mortality if left untreated. Although Q fever is rarely seen among the secondary causes of HLH, it is a treatable disease that should be kept in mind in people who have livestock or in contact.

PP-80

Successful treatment of relapsed and refractory cold agglutinin disease with bortezomib: case report

S. Çelik, Z. Güven, B. Eser, L. Kaynar, M. Çetin, A. Ünal

Erciyes University, Faculty of Medicine, Department of Hematology

Background: Cold agglutinins are antibodies that recognize antigens on erythrocytes at temperatures below normal body temperature. The antibodies are IgM and typically bind to the "I" or "i" antigens on the erythrocytes to form agglutination in the erythrocytes. This causes extravascular hemolysis and results in anemia. Diagnosis is based on positive direct Coombs test for C3d and ≥64 cold agglutinin titer at 4°C with evidence of hemolysis findings such as reticulocytes, high LDH and indirect bilirubin and low haptoglobulin. The treatment approach includes avoiding cold, correcting anemia, reducing antibody production, and treating the underlying disease if there are secondary causes. We present a patient who has been followed up with the diagnosis of Cold Agglutinin Disease (CAD) for about 7 years and did not respond to steroid and rituximab treatment and received a significant response with Bortezomib treatment.

Case report: A 66-year-old male patient who was examined for anemia in September 2012 was diagnosed as CAD because of hemolytic findings, agglutinations in peripheral smear and direct coombs C3d (4+). Prednol treatment was started and the steroid treatment was reduced at regular intervals for about three years and discontinued and restarted. In June 2018, a lung mass was detected and the patient's biopsy was reported as adenocarcinoma. The patient underwent right middle lobectomy and a total of 6000 cGy doses of stereotactic radiosurgery was applied. Hgb 10.4 g/dL, Indirect bilirubin 4.5 mg/dL, Direct coombs C3d (4+), haptoglobulin: 7.5, LDH 406 U/L were detected in the patient whose hemolytic anemia deepened in November 2018. Prednol treatment was restarted. Rituximab treatment was started when the patient's hemolytic anemia did not improve. After the 4th cycle, indirect bilirubin 4.5mg/dL, direct coombs C3d (3+), haptoglobulin 7.5, LDH 406 U/L and widespread agglutination were observed in peripheral smears. Bortezomib 1.3 mg/m^2 treatment was started. At 2 months follow-up, HGB 15.8g/dL, indirect bilirubin 0.5mg/dL, direct coombs C3d (–), haptoglobulin 324, LDH 297 U/L were detected. Significant improvement was observed in the patient's clinic as in the laboratory findings.

Discussion: Primary CAD is a very rare disease, with an incidence and prevalence of 1 per million and 16 per million, respectively. The median age at diagnosis is 67 years (30–92 years).The etiology of secondary CAD includes infections, autoimmune and lymphoproliferative diseases. Clinically, there are cold-related symptoms and anemia symptoms. Treatment should be avoided to reduce cold-induced symptoms and hemolysis. Rituximab is currently the most effective treatment for reducing antibody production. It can be given alone or in combination with bendamustine, interferon alpha, fludarabine and prenizolon. Bortezomib is used when rituximab is ineffective or contraindicated. Bortezomib is a proteasome inhibitor used in B cell lymphoid malignancies and is recommended for use in cases where Rituximab is ineffective or contraindicated. Evidence for the efficacy of Bortezomib comes from a 2018 study involving 21 individuals with CAD who had anemia and chronic hemolysis (hemoglobin <10 g/dL) and for whom at least one prior therapy has been ineffective. Six of 19 evaluable patients (32 percent) had a response (defined as transfusion independence or a 2 g/dL increase and hemoglobin level); the response was complete in three and partial and three. Two different case reports were also consistent with this study.
Conclusion: CAD is a rare autoimmune hemolytic anemia. Rituximab is still the most effective agent in treatment. In cases where rituximab is ineffective, combination therapies and bortezomib are tried. Bortezomib was found to be effective in other case reports and studies as in our case.

PP-81
Diagnosis of transcobalamin deficiency in a patient with pancytopenia: a case report

Y. Yalvaç, S. Durusoy, H. Şahin, M. Pehlivan, V. Okan
Department of Hematology, Gaziantep University Faculty of Medicine

Background: Transcobalamin is a protein that transports cobalamin from the blood into the cell. Transcobalamin II (TC) deficiency is a rare autosomal recessive disorder. The mutation in the TCN2 gene is responsible of the disease. TC deficiency is usually seen in the first year of life. Clinical findings are failure to thrive, diarrhea, vomiting, pancytopenia, megaloblastic anemia, and neurological findings. TC deficiency have elevated homocysteine and methylmalonic acid levels. Treatment with parenteral vitamin B12. We report the patient with pancytopenia who was diagnosed with TC deficiency in our hospital.
Case report: A 29-year-old female patient was admitted to the hematology outpatient clinic with complaints of weakness, fatigue. No history of additional illness. There is no history of drug use or operation. Physical examination, especially in the upper and lower extremities petechiae available. In the tests WBC: 3.5×10^3/µL, HGB 3.8 g/dL, platelet $60{,}000\times10^3$/mL, MCV 100 fl, total bilirubin 2.4 mg/dl, direct bilirubin 0.45 mg/dl, indirect billirubin 2.02 mg/dL, LDH 5,338 U/L. Additional findings of the patients with pancytopenia; B 12 level 11 µg/mL, haptoglobulin 0.51 g/L. Intramuscular injection cyanocobalamin of B12 deficiency treatment was started. After 1 week of treatment, pancytopenia was observed and there was no decrease in complaints. Bone marrow biopsy was performed to rule out possible bone marrow pathologies. Bone marrow aspiration and biopsy showed megaloblastic changes in the erythrocyte series, and the blast rate was 1%. B12 replacement therapy in patients continuing from the more rare cause of urinary methylmalonic acid and homocysteine levels in mind TC deficiency views. Serum homocysteine was 108 µmol/L (0–15), urine methylmalonic acid 1500 mg/g creatinine (0–1000 mg/g creatinine). It was thought that there might be late-onset transcobalamin II deficiency. To confirm the diagnosis of TC deficiency holotranscobalamin II level were studied. Holotranscobalamin level was determined as 18 pmol/L (25–165 pmol/L) and TC deficiency was diagnosed. IM hydroxycobolamine treatment was started. 1 day during the week im hydroxocobalamin-treated patients after 1 week evaluation, the improvement of pancytopenia, was reduced clinical complaints. The patient was first sent to the monthly controls after the week.
Conclusion: In TC deficiency cobalamin cannot be taken into the cell. Clinical symptoms may occur in the absence of cobalamin. The level of deficiency can determine the time of onset of the disease. When the literature is examined, it is seen that the cases were diagnosed in the first few months of life. As in our case, it may take time for the disease to develop in cases of mild deficiency. In the literature, we did not find any cases of TC deficiency diagnosed in advanced age. Our case may be the first case diagnosed with TC deficiency at an advanced age.

PP-82
Exercise program improves quality of life of the patients during the first 100 days following hematopoietic stem cell transplantation

V. Yıldız Kabak[1], H. Goker[2], T. Duger[1]
[1]Hacettepe University, Faculty of Physical Therapy and Rehabilitation, Ankara, Turkey; [2]Hacettepe University, Faculty of Medicine, Department of Hematology, Ankara, Turkey

Objective: The aim of this study was to determine effectiveness of an individual exercise program by starting before hematopoietic stem cell transplantation (HSCT) and was performed through hospitalisation and continued with home exercise program after discharge up to 100 days after transplantation.
Methodology: Totally 50 patients were included in this study and participants were assigned to two groups as intervention group (IG, n=25) and control group (CG, n=25) with simple randomization. Participants were assessed at three time points: before HSCT, at the discharge and at the 100th day after HSCT. For IG, aerobic, muscle strengthening, endurance and stretching exercises were performed through hospitalization and these exercises and walking program were advised as home exercise program after discharge, which was controlled by a physiotherapist at least two times up to 100th day. CG continued their routine care without any physiotherapy service. Quality of life level was assessed by The European Organization of Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ - C30). This questionnaire has three subscales including general health, symptom, and functional score.
Results: The mean age of the participants 51.56±12.22 years for IG and 46.0±16.63 years for CG. Baseline demographic and medical characteristics and quality of live level of the patients were similar in the both groups. At the discharge quality of life level was higher in IG than CG in terms of symptom score (25.22±17.6 vs. 45.06±18.59 points, p=0.009). At the 100th day, it was found that positive effects of the exercise program on quality of life were continued when compared with CG (84.78±15.38 vs. 56.88±26.59 points, p=0.001).
Conclusion: As our knowledge this is the first exercise therapy study which continued up to 100 days following HSCT. This period is important and critical in terms of early side effects due to HSCT. As a result of our study, the exercise program continued up to 100 days after HSCT which is individual and supervised by a physiotherapist improves quality of life throughout HSCT. Exercise programs for individuals undergoing HSCT should be performed dynamically, and planned daily according to the individuals' performance, clinical, and hematologic status.

PP-83
Next-generation sequencing panel in de novo acute myeloid leukemia

A. Bolaman[1], İ. Erdoğdu[2], A. Turgutkaya[1], C. Selim[1], A. Eroglu Kucukerdiler[1], İ. Meteoğlu[2], I. Yavasoglu[1]
[1]Adnan Menderes University, School of Medicine, Department of Hematology, Aydin, Turkey; [2]Adnan Menderes University, School of Medicine, Department of Molecular Pathology, Aydin, Turkey

Objective: Acute myeloid leukemia (AML) is a clonal disease due to genetic aberrations. Next-generation sequencing (NGS) analysis shows the genetic landscape of acute myeloid leukemia (AML). It may be picked out new molecular markers for diagnosis and prognosis. NGS panels now being commercially available in most specialized hematologic laboratories.
Methodology: Bone marrow samples from patients diagnosed with de novo AML were collected in Adnan Menderes University Hospital (Aydin/Turkey) between March 2018 and August 2019. We used commercially the NGS panel that was created for myeloid neoplasms. Bioinformatics tool used in

the variant evaluation was QIAGEN clinical insight interpret. Median unique molecular index coverage was 201×, and quality score (Q-score) >25, 98.27%.
Results: We investigated 128 gene/variant in 40 de novo AML patients. The mutations of 22 related genes were detected by using AML/MDS-NGS chips. The most frequent pathogen gene is KMTA2C1. Other genes with pathogenicity in order of frequency were ASXL1 (15%), DNMT3A (15%), SRSF2 (12.5%), TET2 (10%), CEPBA(5%), ZRS2 (5%).
Conclusion: Our NGS results showed that the most frequently pathogenetic variants are in the KMTA2C1, ASXL1 and DNMTA genes in de-novo AML patients. Pathogenic genes found by NGS method are increasingly important in determining the prognosis and treatment of patients.

Oncology

PP-84
A room of my own

L. Gov Ari-De Vries
Sha'are Zedek Medical Center

Background: Three years ago, a unit for autologous bone marrow transplant for hematological patients has been established in Shaare Zedek Medical Center. The patients meet with the doctors for the treatment plan usually following the diagnosis. From the point of view of a part of the patients, the process appears simple, short term, and promises cure. In reality, the process is long term, including aggressive chemotherapy prior to the transplant. The treatment is highly aggressive and toxic with many physical and mental side effects for the patient and his/her family. The transplant process requires hospital admission for about a month in an isolation room. No one is allowed in the room except for close relatives and the medical staff. The social worker, part of the caring staff, accompanies patients and families from the initial diagnosis through this taxing and stressful process. Most patients are young, average 45 years, in the middle of their careers, from a broad spectrum of occupations, education as well as social status, representing Israeli society.
Aims: 1. To accompany and empower patients by means of giving them tools to cope with the transplantation process which is a crisis situation in the midst of their lives 2. To teach patients self-awareness 3. Promote quality of life for the patients especially during the stay in the isolation room by way of creating a safe domain.
Methodology: The following tools has been utilized: 1. The "Empowerment method": an advanced view of the powers and experiences of patients that constitute resources in addressing crisis. 2. Work of hope: finding unique meaning in life crisis
Results: This work is based on therapeutic conversations that took place inside the isolation room with about30 patients, mostly men; average age was 50, during the past three years. With the understanding that a patient goes from the public sphere to a private one-the isolation room- my entrance into the room was based on the ability and willingness of the patients to go into a treatment dialogue at that point and time. From the narratives of the patients, a few themes were extracted that were repeatedly discussed by most patients. 1. Fear of death 2. Post-traumatic issues 3. Fear of isolation 4. The issue of relationships 5. Mind and body 6. Children 7. Faith 8. Closure As cited by S.A, a 49-year-old man "I'm afraid to give in and die, help me to stay alive. And if I die, I want to know that I have left no unfinished business."
Conclusion: From the therapy sessions it appears that the central issues that bother the patients belong to the private space and the coping with it. The process of treatment helps patients to go from the private sphere back to the public one
Recommendations: It seems essential for the patients in the isolation room, undergoing autologous bone marrow transplant, to have therapy sessions with a qualified social worker as part of the holistic care. 'Having a room of his own' in the process enables an opportunity to examine the inner self esteem and strengths of the patients thereby patients learn to contribute to themselves from themselves.

PP-85
Xanthohumol induce apoptosis through p38 MAPK signaling pathway in human nasopharyngeal cancer cells

M. Lo, D. Chen
Changhua Christian Hospital

Objective: Nasopharyngeal carcinoma (NPC), arising from the squamous mucosal epithelium of the nasopharynx, is a unique malignant head and neck cancer, and it is endemic in a few areas including Southern China, Southeast Asia (Taiwan, Hong Kong, Singapore, and Malaysia), North Africa and the Arctic. With advances in radiation therapy (RT) and chemotherapy strategies, the survival rate of patients with NPC has improved, but the prognosis of patients with NPC remains poor. Therefore, identification of mechanism of drug resistance involved in chemotherapeutic response is critical for predicting tumour response. Xanthohumol, derived from Humulus lupulus, has a wide range of beneficial effects, including anti-angiogenesis and anticancer properties.
Methodology: The aim of the present study was to investigate the effect of xanthohumol in NPC cells and to understand the mechanism of its action.
Results: Our results revealed that the treatment of NPC-039 and NPC-BM cells with xanthohumol potently induce cell apoptosis, and which subsequently activated caspase-3, -8, and -9 and poly (ADP-ribose) polymerase. Moreover, xanthohumol induced apoptosis through the modulation of AKT, p38 mitogen-activated protein kinase, extracellular signal-regulated kinases 1 and 2, and jun N-terminal kinases 1 and 2 pathways.
Conclusion: In summary, our data show that xanthohumol induces apoptosis in human NPC cells and suggesting xanthohumol to be a promising candidate for NPC therapy.

PP-86
Primary Ewing sarcoma of the kidney

E. Abdullayev[1], E. Abdullayev[2], S. Ghani[1], N. Ziegenhagen[1], P. Reichardt[1]
[1]*Helios Klinikum Berlin Buch, Department of Stem Cell Transplantation, Hematology, Oncology and Palliative Medicine, Berlin, Germany;* [2]*Nakhchivan Military Hospital, Department of Intensive Care Unit, Nakhchivan, Azerbaijan*

Objective: Extraskeletal Ewing sarcoma of the kidney (ESK) or primitive neuroectodermal tumor (PNET) is a rare neoplasm, typically presented with irradiating flank pain that mimics the pain associated with kidney stones. Total surgical resection is considered as the treatment of choice for these tumors. However, chemotherapy in the adjuvant setting has also shown promising results.
Case report: A 17-year-old male with complain of pain in the right flank and acute respiratory distress and pain on inhalation. Underwent sonography followed by computed tomography (CT) scan, which revealed large (14×11.5×10.5 9 cm) heterogeneous mass involving the upper and mid pole of the right kidney with large necrotic component and invading the perinephric fat and Expansion into the vena cava inferior (VCI). The patient underwent right nephrectomy. A radical nephrectomy (i.e., adequate resection margins plus lymph node dissection and VCI) was performed. Histopathology revealed a neoplastic lesion composed of large "small, round and blue-celled tumor" in the right kidney with infiltration of the perirenal fat tissue just below the peritoneum, large tumor thrombus in the trunk vein and extension into the vena cava. The lymph nodes examined here are tumor-free. Tumor tissue in the nephrectomy specimen on the upper border of the preparation. Immunohistochemically, the tumor cells express strongly and continuously membranous and partly cytoplasmic the CD99-antigen (MIC2). A small part of the tumor cells CD57 positive. Following further immune reactions than negative: BerEP4, AE1/3, LCA, TdT, CD20, Synaptophysin, Chromogranin, WT1, CD56, Desmin, Myogenin. Ki67 index was 30%. Molecular pathology examination showed ESWSR1-FLI1 Fusion of type II. All these findings were consistent with ESK/PNET. Complete initial diagnostics: Evidence of a tumor residuum or local recurrence in the right kidney lodge, suspected on small thrombus of the VCI caudal of the hepatic veining and small lesion in liver segment V, not clearly assignable. PET whole-body examination showed weak PET-positive herd cutaneous/subcutaneous ventral to the left patella.

A bone marrow biopsy showed no infiltration. The patient was included in the Ewing 2008 study. He has received 6 cycles of chemotherapy according to VIDE protocol. CT-Thorax and MRI-Abdomen after 6 cycles showed constant presentation of the herd-shaped small consolidation in the right upper lobe and micronodular in the left-ventral lower lobe and haemangioma-typical lesion in SWK2. 8 cycles VCA according to the Ewing protocol with different composition. no administration of vincristine more in passenger polyneuropathy. In parallel with 7th cycle radiotherapy. a total of 25 fractions. After the end of chemoradiotherapy in 3 monthly follow-up no indication of relapse.

Conclusion: ESK/PNET is a rare but relatively aggressive renal neoplasm that typically manifests in old children and young adults, as observed in this study. The clinical presentation of ESK/PNET includes flank pain, palpable mass, and hematuria. Histopathology in tandem with immunochemistry has been used to provide a definite diagnosis. Typically, surgery followed by adjuvant chemotherapy is considered as the principal management for ESK/PNET. Radiotherapy has also been employed for the management of ESK/PNET in adjuvant settings.

PP-87

Circulating tumor cells in patients with breast cancer I–III stages

V. Ponomarev[1], O. Chernysheva[2], S. Polikarpova[1], V. Kirsanov[1], E. Bogush[2], N. Tupitsyn[2]

[1]*Sechenov First Moscow State Medical University (Sechenov University);*
[2]*Blokhin National Medical Research Center of Oncology*

Objective: To determine the frequency of CTCs in the early stages of breast cancer I–III stages and their relationship with clinical and morphological factors.

Background: Circulating tumor cells (CTCs) is a population of tumor cells in the peripheral blood as a result of separation from the primary tumor and its intravasation into lymphatic or blood vessels. CTCs can be detected by liquid biopsy in the early stages of breast cancer, and their presence correlates with a high risk of recurrence of the disease. Numerous clinical studies have established the prognostic value of CTCs in the early stages of breast cancer.

Methodology: The study included 47 patients who had breast cancer (median 51 years), who were treated at the "N. N. Blokhin National Medical Research Centre of oncology" of the Health Ministry of Russia in 2015–2017. Determination of the CTC was carried out to all patients before the start of treatment in the laboratory of immunology of hemopoiesis. CTCs were detected immunologically by flow cytometry in 7.5 ml of peripheral blood. Staining was carried out by direct immunofluorescence with monoclonal antibodies to the panleukocyte antigen CD45, the adhesion molecule of epithelial cells EpCam (CD326) and cytokeratin 7 and 8 types - Cam5.2 (Becton Dickenson, USA). Calculation of stained samples was carried out on a FACS Canto II flow cytometer (Becton Dickinson, USA). The analysis of the obtained data was action using the Kaluza Analysis software (Beckman Coulter, USA).

Results: The overall detection rate of CTCs in patients who have breast cancer stage I-III was 85.1% (40 out of 47). Patients were locally advanced and primary resectable breast cancer, CTCs were detected by flow cytofluorimetry with approximately the same frequency: in 21 out of 24 (52.5%) and 19 of 23 patients (47.5%), respectively, the differences were not statistically significant (p=0.7). The frequency of progression in the group of patients with CTCs was 10% (4 of 40 patients). All these patients had stage III breast cancer. Luminal B subtype of breast cancer, CTCs in the peripheral blood was detected significantly more often than in patients with other molecular subtypes (p=0.05). In the group of patients with identified CTCs, a tendency to an increase in tumors with the degree of malignancy G2 was 77.5%, compared to the degree of malignancy G3 22.5% (p=0.08). With the other clinical and morphological characteristics, reliable statistical significance was not found.

Conclusion: Existing prognostic factors of breast cancer can be supplemented with the determination of CTCs using liquid biopsy. The presence of these cells in the peripheral blood of patients with primary operable and locally advanced breast cancer suggests a possible primary disseminated process. Determination of CTCs is associated with certain morphological factors in breast cancer tumor that requires further research with a larger sample

PP-88

Behavior and outcomes of pregnancy associated breast cancer: a cohort study

A. Osmani

Oncology Centre, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudia Arabia

Objective: Pregnancy-associated breast cancer (PABC) is associated with poor prognosis and a decreased overall survival. A retrospective review was conducted to review the experience and outcome in a tertiary care hospital, and to compare those seen in a matched group for year of diagnosis.

Methodology: This is a retrospective review of a prospectively collected breast cancer registry. The study was conducted in a tertiary care hospital in Riyadh, Saudi Arabia from January to December 2014. Female patients with PABC were identified and matched with similar cohort of non-pregnant breast cancer patients that were diagnosed between 2001–2010. Clinical data including age, tumor biology, clinical stage, follow up and outcomes (disease free survival, DFS) were analyzed and compared between the two groups using SAS 9.3 and R-2.14.1

Results: A total of 110 patients in Group 1 and 114 patients in Group II were analyzed. In both groups, the patient age ranged was between 20 to 45 years; the median follow-up was 34 months in PABC and 54 months in non-pregnant cohort. PABC were statistically more likely to be triple negative (p value 0.05) and diagnosed at advanced stage (stage 3 and 4) (p value 0.02). There was no difference in the occurrence of Her-2 positive disease. In pregnant patients there was a 5-year survival rate of 65% compared to non-pregnant cohort of 82% with p value of 0.002 and DFS was also 47.5% versus 65.4% with a p value.002 which is statistically significant.

Conclusion: Pregnancy associated breast cancer (PABC) is diagnosed at a more advanced stage and tends to be triple negative and they are associated with a worse DFS and overall survival. Early detection during pregnancy may improve outcome.

PP-89

Bad disease with reasonable outcomes: case report metastatic breast cancer with bone marrow and leptomeningeal disease

A. Osmani

Oncology Centre, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudia Arabia

Case report: Breast cancer with an abnormally high expression of HER2 on its cell surface is characterised by a more aggressive tumor biology, with adverse prognosis. Median survival time of breast cancer after the diagnosis with apparent bone marrow metastasis is few months. Breast cancer also constitutes 2–5% patients with leptomeningeal carcinomatosis. Unfortunately, even with multimodality therapy, the median survival is only 12 weeks; although in one series, patients live an average of 7.5 months after diagnosis. A 35-year pre-menopausal lady presented to hematology clinic in September 2015 with anemia and worsening lower backache radiating to lower limbs without neurological deficit for two months. There are no other constitutional symptoms or family history of malignancy. Her baseline investigations revealed low hemoglobin. She underwent bone marrow biopsy, which revealed heavy infiltration by metastatic glandular cells with some areas of normal tri-lineage hematopoiesis. Immunohistochemistry was positive for cytokeratin 7 (adenocarcinoma), most likely the breast primary malignancy. She was referred to oncology department for further management. CT scan revealed liver studded with multiple small irregular hypodense lesions, minimally enhancing irregular lesion seen in the right medial breast and multiple osseous lytic bone lesions without fracture. Later, MRI spine showed irregular diffuse metastatic involvement of multiple vertebral bodies with no evidence of cord compression. PET CT scan revealed hypermetabolic disease in multiple bones, liver and right breast and left axillary nodes. Mammogram showed irregular, spiculated mass 1.6 cm at the lower inner quadrant of

the right breast with minimal distortion, BIRAD 5. Biopsy of breast lesion revealed IDC grade 2, estrogen and progesterone receptors negative, and HER-2/neu overexpression 3+ positive, FISH positive and Ki 67 of 20%. She was treated with palliative radiation to the thoracolumbar spine and after its completion was started on combination of chemotherapy with dual anti HER-2/neu therapy with docetaxel, pertuzumab, trastuzumab and zoledronic acid as part of systemic treatment. Subsequent PET CT scan, after completion of three cycles showed complete metabolic resolution. After completion of six cycles, bone marrow biopsy revealed cellular marrow with no morphological evidence of disease. She was continued on maintenance therapy with dual anti HER2 therapy and zoledronic acid for more than a year. In March 2017, she presented with short history of diplopia and dizziness. On examination, there was no peripheral vision in right eye, with normal vision in left eye. MRI brain showed evidence of leptomeningeal metastasis. She received whole brain radiation of 30 Gy over 10 fractions and planned for intrathecal trastuzumab via Ommaya reservoir. She received her first intrathecal dose but unfortunately developed immediate complication, which recovered with conservative management. Later, it was decided to omit intrathecal trastuzumab and to continue with trastuzumab and zoledronic acid. Her subsequent and recent brain imaging revealed improvement in CNS disease; whereas, systemic imaging revealed stable disease. It has been for more than two years from the time of initial diagnosis that patient is doing well with good performance status, tolerating the treatment and the systemic disease is well controlled on maintenance therapy.

PP-90

Proptosis of eye: an unusual presentation of genitourinary malignancy: case report on prostate cancer

Q. Saleem
Department of Ophthalmology, Jinnah Postgraduate Medical Centre

Background: Orbital metastasis is a rare occurrence found only in about 3–10% of all prostate cancers.
Case report: A 72 years male presented with proptosis of the left eye associated with pain, blurred vision and frequent headaches which was progressive in nature for the past 8 months. Past medical history was consistent with bladder outflow obstruction since 3 years. MRI brain and orbit with gadolinium was done which revealed a large soft tissue mass measuring 7.5×4.0 cm in the left frontal region involving the skull vault and extraclavarial region. Intracranial infiltration was also seen. The mass was occupying the left side of the orbit, obscuring the lacrimal gland, recti muscles abducting the eyeball. However, no infiltration was found in bulbus occuli. There was no evidence of haemorrhage or infarction in the brain. With the intent of preserving the patient's sight, surgery was performed. The intracranial mass was removed in order to achieve palliation. Histopathology of the specimen revealed poorly differentiated malignant neoplasm favouring metastatic carcinoma. Immunohistochemistry showed positivity for cytokeratin AE1/AE3 and CD 10. Cytokeratin CAM 5.2 was diffuse strong positive. LCA, Desmin, Neurofilament, CD 138, Synaptophysin, Cytokeratin 7, Cytokeratin 20, p63, GFAP and Vimentin were found to be negative. EMA stain was non-contributory. Postoperative radiotherapy was administered with a palliative intent. Primary site of the tumor was not discernible without clinical correlation. CT chest, abdomen and pelvis identified an enlarged prostate with a nodular lesion. Left pelvic, para aortic and mediastinal lymphadenopathy was also seen. A soft tissue density lesion was found in the left lung apex, involving the pleura. Serum PSA level was 149 μg/L. Bone scan showed increased tracer uptake involving the superior margin of left orbit with photon deficient area involving frontal bone. Focal areas of increased tracer uptake were noted over left sided 3rd rib, right sided 5th rib anteriorly and trochanteric region left femur. Hormonal treatment with androgen deprivation therapy along with intravenous bisphosphonates was commenced later.

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Pediatric nasopharyngeal mass: a case report

H. Sarbay[1], A. Atay[1], B. Malbora[1], E. Petmezci[2], T. Atasever Rezanko[3], Z. Gezginadam[4], M. Şalvız[4], N. Bakar[5], T. Atay[6]
[1]TC Yeni Yuzyil University Faculty of Medicine Pediatric Hematology and Oncology; [2]TC Yeni Yuzyil University Faculty of Medicine Pediatric Intensive Care Unit; [3]TC Yeni Yuzyil University Faculty of Medicine Pathology; [4]TC Yeni Yuzyil University Faculty of Medicine Otolaryngology head and neck surgery; [5]TC Yeni Yuzyil University Faculty of Medicine Radiology; [6]TC Yeni Yuzyil University Faculty of Medicine Pediatrics

Background: Nasopharyngeal carcinoma is a rare tumor in children and is usually seen in adolescence. It is distinguished from the adult form of the disease by its association with Epstein–Barr virüs (EBV) infection, undifferentiated histology, and high incidence of advanced locoregional compromise. EBV is detected mostly in all nonkeratinizing nasopharyngeal carcinoma. Epistaxis, nasal congestion, trismus, otitis media are the most common initial signs and symptoms. Cranial nerve paralysis occurs when the disease spreads to the oropharynx and skull base. In this article, a pediatric patient diagnosed as nasopharyngeal carcinoma is presented because of its rarity in this age group.
Case report: A 2-year-old male patient who had dyspnea and swallowing 3 months ago developed respiratory distress within 1 month. The patient was admitted to the intensive care unit and intubated and connected to a mechanical ventilator. MRI and CT showed a nasopharyngeal mass. The patient was referred to us with an increase in mass size during follow-up, worsening in general condition and needing cardiopulmonary resuscitation twice. The patient was admitted to intensive care unit. His general condition was poor, intubated, massive swelling of the neck and lower jaw. Laboratory evaluation revealed WBC: 39,710/mm^3, neut: 34,840/mm^3, hgb: 9.4 g/dl, plt: 192,000/mm^3, CRP: 135 mg/L, and liver and kidney function tests were normal. His electrolytes were normal except mild hyponatremia and hypopotasemia. Enterobacter Cloacae Complex was isolated in the first blood culture of the patient. Multiple antibiotic resistance microorganisms were started. MR imaging revealed multiple pathological masses and bilateral nodes in the posterior cervical region extending from the nasopharyngeal region to the cavernous sinuses, to the posterior ethmoid bone, to the maxillary sinus, infiltrating the sphenoid sinus, infiltrating both intracanalicular segments of the optic nerve, and invading the prevertebral fascia. Biopsy was performed after tracheostomy was performed. Non-keratinized nasopharyngeal carcinoma was evaluated as undifferentiated subtype. EBV VCA IgG result was positive. Grade 4 (T4-N2) was accepted according to AJCC staging system. ARAR0331 Cisplatin and 5-flurouracil were started according to the treatment protocol. After the first chemotherapy, there was a significant reduction in mass size. Tumor fragments of 3–4 cm necrotic hemorrhage were spilled from the mouth. After treatment, intermittent massive bleeding foci developed in the oral and nasal mucosa due to tumor necrosis. Local medical and surgical intervention was performed. On the second week of the treatment, febrile neutropenia developed. The patient did not respond to antibiotic and supportive therapy and died due to multiorgan failure.
Conclusion: Although nasopharyngeal carcinoma is a rare tumor in childhood, it should be included in the differential diagnosis in children with neck mass. It is thought that early diagnosis and treatment increase the success of the treatment and decrease the mortality due to the stage of the disease.

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A boy with xeroderma pigmentosum and multiple types of skin cancer

H. Sarbay[1], Z. Rizvanovic[2], T. Atasever Rezanko[3], Ş. Yılmaz[4], B. Coşan Sarbay[5], B. Malbora[1], A. Atay[1]

[1]TC Yeni Yuzyil University Faculty of Medicine Pediatric Hematology and Oncology; [2]TC Yeni Yuzyil University Faculty of Medicine Plastic and Reconstructive Surgery; [3]TC Yeni Yuzyil University Faculty of Medicine Pathology; [4]TC Yeni Yuzyil University Faculty of Medicine Radiology; [5]Kanuni Sultan Süleyman Education and Research Hospital Pathology

Background: Xeroderma pigmentosa is inherited as an autosomal recessive disorder that presents with photosensitivity and premalignant cutaneous pigmentary changes. The disorder of DNA damage repair affect tumor suppressor genes. Consequently, fatal skin cancers develop. Malignant melanoma, basal cell carcinoma and squamous cell carcinoma are the most common cancers. The average age of skin cancers is 8 years. Eye involvement can be seen in 40% of the patients. Corneal keratitis, ulceration, band keratopathy, squamous cell carcinoma may develop. In this article, a patient with Xeroderma pigmentosum whom different types of skin cancers were detected was presented due to its rarity.

Case report: A 7-year-old male patient with Xeroderma pigmentosum was admitted to the external center with a mass in his left eye. After radical excision of the left eyeball, pathological examination revealed a well-differentiated squamous cell carcinoma. The patient presented with facial lesions during follow-up. Masses of 0.5–1 cm in size were excised under the forehead, nose, right cheek, left cheek, both ears and anterior, left eye. The pathology of the samples taken from the skin of the forehead, left ear, left eye and the skin of the nose was reported as squamous cell carcinoma. The pathology of the samples taken from the right auricle and right cheek skin was reported as basal cell carcinoma. However, pathological results of the specimens obtained from different lesions on the nasal back and right cheek were reported as seborrheic keratosis. The patient was consulted to the pediatric oncology department. His general condition was good, and his physical examination was normal. In laboratory evaluation, wbc: 5,750/mm^3, neutral: 1,470/mm^3, hgb: 13, plt: 255,000/mm^3, liver and kidney function tests were within normal limits. No organomegaly-lymphadenomegaly mass was seen on abdominal USG. Cranial and orbital MRI showed no evidence of tumor tissue other than post-operative changes in the left orbital. The patient was followed up with the current findings. PET-CT control is planned.

Conclusion: In conclusion, xeroderma pigmentosum is a rare disease with chronic skin manifestations, eye involvement and malignant transformation. Early diagnosis of the disease and early consultation to the relevant departments are particularly important for the early diagnosis and treatment of malignant lesions in terms of preventing mortality and morbidity.

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Asbestos-related malign mesothelioma: a single-center experience

M. Simsek[1], U. Isik[2]

[1]Yozgat City Hospital; [2]Kocaeli University

Objective: Malignant mesothelioma is an aggressive malignancy and originates from the mesothelial cells present in pleura (~70%), peritoneum (~30%), abdominal cavity, pericardium, omentum, mesenterium, and tunica vaginalis. Also it is a very rare entity with a prevalence of less than 1% of all cancers; it has a dismal prognosis. Overall survival was reported between 6 months to 18 months with a median period of 12 months. The most important underlying reason of malign pleural mesothelioma was established to be previous asbestos exposure. Development of disease after initiation of exposure takes a long time period approximately 30-40 years. Malign mesothelioma has four histological subtypes; epithelioid, sarcomatoid, desmoplastic, and biphasic. The foremost predictor of survival was defined as histological subtype. Fortunately, the most common subtype is epithelioid and it has the best survival outcomes. Diagnosis at advanced stage in most of the cases makes this disease incurable and systemic chemotherapy emerges as the only effective treatment option. Nearly all patients face disease progression and no standard agents are present for this setting. We aimed to evaluate the demographical features and outcomes of our patients with diagnosis of malign mesothelioma.

Methodology: We retrospectively analyzed the data of malign mesothelioma patients between January 2009 and July 2019 referred to our clinic. 16 patients diagnosed with malign mesothelioma were included in our study. Data were collected from patient files and digital data processing system.

Results: None of the patients in our study had a history of occupational asbestos exposure. Median age was determined as 66.5 (33–75) for our patients. There were three male and thirteen female patients. Of the patients, three had peritoneal mesothelioma and thirteen had pleural mesothelioma. There was one mixed and thirteen epithelioid malign mesotheliomas in our patients. The most preferred first-line treatment was pemetrexed-cisplatin combination and the most common second-line therapy was single agent gemcitabine. Of the six patients that are still alive, two did not have disease progression and treatments of other four patients are still ongoing. For patients with stage 4 disease and that passed away, median progression free survival was 6 months and median overall survival was 18 months. For locally advanced disease, median progression free survival was 16.6 months. Because most of these patients are still alive, overall survival was not calculated.

Conclusion: In this study we aimed to analyze the data of malign mesothelioma patients from an endemic region of Turkey because of asbestos in the soil. Low number of patients was due to low incidence of malign mesothelioma and low population number of this district. Data collection with future studies from different regions will help to prevent disease occurrence and ascertain more effective treatment strategies leading better outcomes.

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Misleading metastatic cystic brain with raised inflammatory markers in undiagnosed NSCLC

A. Malek[1], M. Eddeb[2], M. Benabdullah[3], H. Ahmed[4]

[1]Emitiga Hospital; [2]Tripoli Medical Centre; [3]Tripoli Central Hospital; [4]Tripoli University

Objective: To describe the clinical and radiology presentation of cystic brain metastasis in a patient with non-small cell lung cancer.

Case report: We present a case of multiple cystic brain metastases associated with non-small cell lung cancer (NSCLC). In this case, an old Gentleman who was brought by his family to the emergency department with acute neurological deficit was found to be Febrile. Further workup revealed an increase in patient's inflammatory markers and further findings by an MRI-brain were suggestive for cystic brains lesion and advised by the Radiologist to exclude Tuberculoma and other infectious diseases sharing the same characters. He is a 64-year-old Libyan male presented to the ER with fever, sudden headache, blurred vision and neurological deficit (bilateral upper and lower weakness). His past medical history is significant for diabetes mellitus on insulin. Social history reported that he was an ex-smoker for 35 years. Neurological examination demonstrated bilateral upper and lower limb weakness associated with ataxic gait. Chest x-ray was negative and Routine investigations have been done which showed leukocytosis and a dramatic increase in CRP and ESR. The patient received a broad-spectrum antibiotic, and although there was an improvement in the inflammatory markers, his neurological deficit had been worsened. An MRI brain showed multiple cavitary lesions seen throughout the cerebral parenchyma, the largest one was in the left parietal lobe with surrounding edema, which was initially suspected as Tuberculoma. Therefore, Blood culture and sputum analysis were ordered; However, they returned negative. Tumor markers (TPSA, FPSA, CEA and CA 19.9) have been done which returned normal except for the CEA which showed a significant elevation (132.9 ng/ml). CT scan of chest, abdomen and pelvis showed a right upper lobe lung nodule with no other metastasis elsewhere. A lung biopsy obtained by bronchoscopy was positive for NSCLC. Patient was started on systemic chemotherapy and received palliative whole brain irradiation (WBI).

Results: An MRI brain showed multiple cavitary lesions seen throughout the cerebral parenchyma, the largest one was in the left parietal lobe with surrounding edema, which was initially suspected as Tuberculoma. Tumor markers (TPSA, FPSA, CEA and CA 19.9) have been done which returned

normal except for the CEA which showed a significant elevation (132.9 ng/ml). CT scan of chest, abdomen and pelvis showed a right upper lobe lung nodule with no other metastasis elsewhere. A lung biopsy obtained by bronchoscopy was positive for NSCLC.

Conclusion: Metastatic cystic brain lesions remain relatively unusual. Although the pathogenesis is yet unclear but the incidence is rising due to the increase in the survival rate as well as many cancers remains un diagnosed over long period of time. In addition to that, lung cancer has been reported as the most common origin of brain metastases with breast cancer coming in second and pancreas, kidney and even melanoma, in order. On the other hand, cystic brain lesions may be

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The ratio of hemoglobin-to-red cell distribution width could predict survival in advanced pancreatic adenocarcinoma

C. Mirili
Department of Medical Oncology, Ataturk University Faculty of Medicine

Objective: Pancreatic cancer (PC) is ranked as the 14th most common cancer and the 7th highest cause of cancer mortality in the world. Although targeted therapy and immunotherapy agents have prolonged the survival of many cancer types in recent years, the results of PC are still not satisfactory. Therefore, it is very important to identify new biomarkers predicting patients who survive longer. Complete blood count (CBC) is a routine examination performed in cancer patients. Recently, the hematological parameters included in CBC have been shown to have prognostic significance in several cancer. for example, the hemoglobin (HB) level, platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR). Red blood cell distribution width (RDW) is another CBC parameter and shows the heterogeneity in the size of circulating erythrocytes and reflects impaired erythropoiesis and abnormal red blood cell survival but it correlates also with inflammation, undernutrition and impaired renal function, with inadequate production of erythropoietin. Although there are studies showing the prognostic significance of both hemoglobin and RDW in PC, there is no information about hemoglobin to RDW ratio (HRR) in the literature. Therefore, we wanted to demonstrate the prognostic significance of HRR in advanced pancreatic cancer patients

Methodology: Data of 100 patients with TNM Stage III-IV pancreatic adenocarcinoma were evaluated retrospectively. Associations between clinical and histopathological parameters with overall survival (OS) and progression free survival (PFS) were analyzed using Kaplan- Meier curves and compared by the log-rank test. The optimal cutoff values were determined by a receiver operating characteristic (ROC) curve analysis. RDW and HRR were grouped based on a cutoff point 13,7 and 0,91 respectively.

Results: The median age of the patients was 63 (38–85) years and 59 of them were male. According to the TNM staging system, 47 patients were stage 3, 53 patients were stage 4, and 34 of the patients underwent curative surgery. The most commonly used treatment regimen was gemcitabine + cisplatin (45%), with the most common metastasis to the liver (35%). The median PFS and OS are 7 months and 10 months. Although there was no difference in length of life between genders, both PFS and OS were longer in patients with good ECOG performance score (0–1), underwent curative surgery, TNM stage III, low RDW (<13.7) and high HRR (≥0.1).

Conclusion: Both hemoglobin and RDW can be affected by iron, folic acid and vitamin B12 conditions other than cancer. Therefore, it is thought that HRR may minimize any potential bias and may be used as a parameter more reliable than either hemoglobin or RDW. In our study, it was found for the first time in the literature that advanced PC patients with high HRR had longer PFS and OS. Thus, HRR may be used as an inexpensive, easy and feasible prognostic factor in clinical practice in patients with advanced PC.

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Outcomes of a newly formed multidisciplinary retinoblastoma service

A. Butt, I. Jeeva, S. Masud, Z. Fadoo
Aga Khan University Hospital

Objective: Retinoblastoma is the most common intraocular malignancy of childhood, accounting for 3–4% of all pediatric neoplasms. Mortality associated with retinoblastoma in the developed world is 3–5% whereas in the developing world it is 40–70%. There is scarcity of research about retinoblastoma in Pakistan. This study aims to study the presentation of retinoblastoma and impact of multidisciplinary management and tumor board discussions on its treatment at a tertiary care hospital in Pakistan

Methodology: A total of 35 eyes of 26 patients were studied. Retrospective review of retinoblastoma cases presenting to Aga Khan University Hospital from May 2016 to April 2018 was carried out. Demographics were collected form case files that included age, gender and socioeconomic background. Clinical data collected were laterality, intraocular stage, main symptom and clinical sign on presentation as well as treatment given.

Results: A total of 35 eyes of 26 patients were studied. 57.7% (n=15) of the population were males. The age range was 1–84 months (median: 14.5 months). The children presented from 3 different countries. The most prevalent symptom was leucocoria (38.5%, n=10) followed by decreased visual response (15.4%, n=4) and squint (15.4%, n=4). Most of the eyes (57.1%, n=20) were Group E, followed by Group D (20%, n=7) and 17.1% (n=6) Group B. One eye each presented with Group C and A. Tumor board changed management in 37.1% cases. Treatment refusal happened in 3 (11.5%) cases. 54.3% (n=19) of the eyes were treated with combination therapy including enucleation, focal lasers and systemic chemotherapy, 20% (n=7) with only focal lasers and 17% (n=6) with only enucleation. One patient died.

Conclusion: Late presentation remains a problem as is the case in most developing countries. Multidisciplinary care provided by collaboration of ophthalmologists, pediatric oncologists, radiation oncologists, histopathologist and radiologists is important for retinoblastoma cases. Alterations in staging/diagnosis and management, earlier start of treatment, continuity of care, improved survival and adherence to best practice guidelines are all corollaries of multidisciplinary tumor board meetings (MDTMs). Tumor board had an important impact on management by changing treatment plans in 37.1% cases. This is the first study evaluating the impact of MDTMs on retinoblastoma management. Moreover, special emphasis was placed on counselling of parents to prevent treatment abandonment due to financial constraints and hesitancy to enucleate. Our treatment refusal rate was 11.5% compared to 44% in another Pakistani study and 49.5% in a study from India. The mortality in our study was 3.85% while another study from Pakistan reported it as 13%. Awareness needs to be created for early detection of this devastating disease. Efforts should be made to set up more ophthalmic tumor boards and ensure that retinoblastoma patients receive multidisciplinary care.

PP-97

Orbital tumor board: life saver or time waster?

A. Butt, I. Jeeva, S. Masud, Z. Fadoo, S. Altaf, N. Mushtaq
Aga Khan University Hospital

Objective: Orbital tumour board is a multidisciplinary approach towards ophthalmic cancer management, where relevant experts collaborate to manage patients holistically. Studies corroborate the notion that tumor boards positively affect patient outcomes. However, there is a scarcity of literature on the influence of orbital tumor boards globally and about tumor boards in general in Pakistan. There is no existing literature about orbital tumor boards in Pakistan. This study aims to assess the impact of tumor boards in managing ophthalmic cancers.

Methodology: A total of 80 patients were included in the study. A retrospective review of data was carried out on cases that were presented in the orbital tumor board of Aga Khan University Hospital, the first orbital tumour board in Pakistan, from its commencement in August 2017 to May 2018.

Results: Out of a total of 80 patients in the study, 40% (n=32)were female and 60% (n=48) were male. The age of the patients ranged from 4 months to 78 years, with mean of 30 years. For analysis we divided the patients in three groups according to the nature of the diagnosis. Group 1 included those who had malignant tumours 40% (n=32), group 2 were those with benign tumours 30% (n=24) and group 3 was the non-tumour group who were eventually diagnosed with other conditions 30% (n=24). Overall, 31.25% (n= 25) patients had a change in management plan, which was recorded, which included 10 patients in the malignant group, 9 in the benign group and 6 in the non-tumour group.
Conclusion: The study shows that the management of ophthalmic cancers is influenced positively by tumour board discussions.

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Breast cancer distribution in northwest Iran (East Azerbaijan province): results of a population-based cancer registry

S. Pashaie[1], R. Dolatkhah[2], M. Somi[2], R. Asghari[1]
[1]Urmia University of Medical Sciences; [2]Tabriz University of Medical Sciences

Objective: Breast cancer (BC) is the second most common cancer in the world and is the most common cancer in Iran in both sexes. Worldwide, there were about 2.1 million newly diagnosed female breast cancer cases in 2018, accounting for almost 1 in 4 cancer cases among women. East Azerbaijan is the largest and most populous province in the northwest of Iran, which more than 95% of the population is of Azeri ethnicity. The aim of this study was to provide recent data on the BC incidence and distribution in East Azerbaijan, Iran.
Methodology: Data of the patients diagnosed with confirmed BC as registered in the East Azerbaijan population based cancer registry between 2015 and 2017, were linked to the main data sources. The age standardized incidence rates (ASIRs) for BC were estimated.
Results: We had overall 1,410 primary breast cancer cases during two years, in both sexes, which accounted 10.3% of cancer cases. The mean age of our patients was 51.07±13.29, with the age range of 21 to 99 years old. About 98.2% of BC was female, and 1.7% of them were male. The most common morphology was ductal carcinoma (n=1,077, 76.4%), and most of our BC patient were in grade II of disease (35.9%). In 31.2% of patients had lymphatic Invasion, 17.8% vascular invasion, and 8.7% of them had neural invasion. Also, our results showed that breast cancer was the most common cancer among female, with slightly increasing of ASRs from 31.1 to 31.7 per 100,000 women during 2 years. There were two age peaks of ASRs in women, first in approximately 45–55 years and second in 60–70 years old groups.
Conclusion: We observed slightly increase in incidence of BC, which might be explained by the improvement of compliance to the cancer registration, compared with previous reports of our region. However, the low tumor stages and improved knowledge and attitude of women to early diagnosis and screening, which we have recently addressed in our ongoing screening programs in the province, may have played important roles in these results.

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A case with a late recurring limited stage small cell lung cancer

B. Karaalioglu[1], G. Utkan[1], M. Gürbüz[1], P. Kubilay[1], E. Yekedüz[2], M. Büyükkıroğlu[3], C. Erkuşakçı[3], C. Aykaç[4], S. Öztürk[4]
[1]Ankara University Faculty of Medicine Department of Medical Oncology; [2]Ankara University Faculty of Medicine Department of Medical Oncology; [3]Ankara University Faculty of Medicine Department of Internal Medicine; [4]Ankara University Faculty of Medicine

Background: Despite giving a positive reaction to chemotherapy and radiotherapy, small cell lung cancer has a quite low rating of being cured. The expected life expectancy in patients who are under treatment with limited stage small cell lung cancer(LS-SCLC) is approximately two years and the majority of the patients are lost due to recurrence. Although the development of new chemotherapy agents, adding simultaneous radiotherapy to chemotherapy, and application of prophylactic cranial radiotherapy have contributed to survival in patients with limited stage small cell lung cancer, it is revealed that the 5-year survival rate is less than 25%. Our case was diagnosed as late recurrence of LS-SCLC. This late recurrence after response makes the case interesting.
Case report: A sixty-nine-year-old male patient with a history of 100 pack years of smoking admitted to Ankara Atatürk Training and Research Hospital (T.R.H) with complaints of shortness of breath and cough beginning in March 2010. The posteroanterior chest X-ray revealed a right hilar mass. On the thorax computed tomography (CT) taken on 28.04.2010; A 58×50×61 mm sized, solid tumor lesion in the right hilar region, which is compatible with lung carcinoma, obliterating the middle segment branch of main right bronchus, causing total collapse in the middle lobe of the right lung and invading the mediastinum. Lymphadenopathy (LAP) with up to 28 mm in diameter at the subcarinal level and LAP up to 13 mm in the right hilar region were observed. Biopsy was taken from the mass seen at the right middle lobe entrance on bronchoscopy and the report of Ankara Atatürk T.R.H dated 24.05.2010 was evaluated as SCLC. No metastasis was detected so the patient was diagnosed with limited-stage SCLC. The patient was given 3 cycles of cisplatin etoposide therapy. Then, three more courses of cisplatin etoposide were given to the thoracic cavity at the same time with radiotherapy. Prophylactic cranial radiotherapy was applied between 17.03.2011–08.04.2011. The patient was scheduled for follow-up. The result of TAP-CT on 31.07.2018 was reported as following; Right hilar mass. On 30.04.2019, the right lung lower lobe transthoracic fine needle aspiration biopsy and cell block pathology at Ankara University Medical Faculty found the consistency with small cell carcinoma infiltration. Thorax CT of 01.07.2019 showed progressive disease and within normal cranial CT, the patient was accepted to have limited stage SCLC with local recurrence 9 years after the initial diagnosis.
Conclusion: In such cases, it is always possible that the tumor may recur within a short time after the treatment of tumor. However, in this case the patient did not show any signs of recurrence for a long time. After 9 years of disease-free period, the recurrence of the tumor had happened in the patient. The unexpected recurrence of the tumor after such a long time makes the case very interesting.

PP-100

Prognostic value of pretreatment systemic inflammation index in metastatic lung adenocarcinoma

H. Yeşil Çınkır
Gaziantep University Faculty of Medicine

Objective: Systemic inflammation has been reported to play a critical role in the pathogenesis and progression of cancer. Pretreatment serum-based inflammatory biomarkers, such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR) have shown potential prognostic values in a variety of tumors. There is no widely accepted optimal value for circulating blood cell-based biomarkers and no established scoring system that integrates the biomarkers to refine the prognostic prediction for cancer patients. The purpose of this study was to examine the prognostic value of the combination of albumin level and LMR for pretreatment of metastatic lung adenocarcinoma.
Methodology: In this study, patients who received chemotherapy with metastatic stage between February 2011 and October 2017 were evaluated retrospectively. Patients routinely underwent blood testing during the 7 days before chemotherapy. These included the complete blood count and albumin level. The cutoff values (median value) were 2.4 for LMR and 3.9 g/dl for albumin. The SII was defined as follows: patients with Alb level <3.9 g/dl and LMR <2.4 were assigned a group of 1; patients with either Alb level ≥3.9 g/dl or LMR ≥2.4 were assigned a group of 2; and patients with both Alb level ≥3.9 g/dl and LMR ≥2.4 were assigned a group of 3. Overall survival (OS) was defined as the time from initiation of chemotherapy to death from any cause or date of the last follow-up. Progression-free survival (PFS) was defined as the time from initiation of chemotherapy to progression or last follow-up. Survival curves were constructed according to the Kaplan–Meier method, and differences between curves were analyzed using the log-rank test.
Results: Totally, 107 patients were included in the study. The median age was 58 years (range, 21–74). There were 98 (91.6%) males and 9 (8.4%) females.

The most common sites of metastasis were lymph node, bone and liver. The most commonly used chemotherapy regimen was pemetrexed-platinum (59.8%). The median PFS for all patients was 3.9 months (95% CI 3.1–4.8). Median PFS were for groups; 1.9 months (95% CI 1.0–2.8) for group 1; 3.8 months (95% CI 3.09–4.5) for group 2; 6.6 months (95% CI 3.7–9.5) for group 3. There was statistically significant difference between groups (p=0.011). The median OS was 12.2 months (95% CI 8.9–15.5) for all patients. Median OS were for groups; 8.3 months (95% CI 4.6–11.9) for group 1; 12.4 months (95% CI 6.2–18.5) for group 2 and 17.3 months (95% CI 8.8–25.9) for group 3. There was statistically significant difference between the groups (p=0.003).
Conclusion: Albumin and LMR were both influences of nutritional status and systemic inflammation on the prognosis of tumors. This inflammation index system appears to be cost-effective prognostic factor, and can adapted in the clinical practice to stratify the patients for future clinical trials.

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Synergistic effect of turmeric (Curcuma longa) and ginger (Zingiber officinale) plant extracts on the apoptotic behaviour of hepatocellular carcinoma (Hep-G2) cell lines

F. Kabadaş[1], İ. Akalın[2], A. Demirci[1], S. Aşkın[1], S. Akşahin[2], S. Yıldırım[3]
[1]Kartal Anatolian Imam Hatip High School, Istanbul, Turkey; [2]Istanbul Medeniyet University, Faculty of Medicine, Department of Medical Genetics, Istanbul, Turkey; [3]Istanbul Medeniyet University, Faculty of Medicine, Istanbul, Turkey

Background: Hepatocellular carcinoma (HCC) is the most common primary liver malignancy that leads cancer-related deaths worldwide. Although chemotherapy has been used in the treatment, severe side effects on healthy tissues diminish their utility. Therefore, alternative herbicidal reagents inducing apoptosis are being tested in cancer cells and their molecular mechanisms were yet to be clarified. Here we investigated apoptotic effects of active ingredients of Curcuma longa and Zingiber officinale plant extracts on HCC cell lines through pH changes.
Aim: The main purpose of this study is to investigate the correlation between the active ingredients of Curcuma longa (turmeric) and Zingiber officinale (ginger) plant extracts, which are known to have anti-inflammatory, low toxicity, anti-cancer and lipid-lowering effects, and oxidative stress to find out the pathways effecting the apoptosis on Hep-G2 cell line.
Methodology: In order to obtain plant extracts, the plants was crushed in mortar. 5 ml Curcuma longa extract was obtained from 500 g turmeric root and 30 ml Zingiber officinale extract was obtained from 1 root ginger. The extracts were applied as incremental doses (5, 10, 20, 50, 100 µl/2 ml) to each 3×10^5 cell seeded wells in independent experimental setups. Apoptosis analyzes were done by light microscopy evaluations. The therapeutic dosages that induces apoptosis on Hep-G2 cells were set at as 20 µl for turmeric, 50 µl for ginger and 20 µl for synergic effects. Repeated dosages were administered daily for accuracy of the results. Then, two separate measurement steps were applied for each plant extract in 1000 µl of media, where Hep-G2 cells were seeded in the medium and only the medium with plant extracts as control. Then pH of each well is measured using pH meter (HI 2221 Calibration Check pH/ORP Meter, Hanna Instruments).
Results: 0.21 pH elevated in the wells, which are cell seeded and Curcuma longa extract was applied, compared to cell-free medium. 0.15 pH elevated in the wells, which are cell seeded and Zingiber officinale extract was applied, compared to cell-free medium. 0.02 pH elevated in the wells, which are cell seeded and Curcuma longa/Zingiber officinale extract was applied, compared to cell-free medium
Conclusion: As a consequence, pH increment between cellular and non-cellular environments might be caused by intercellular activities. Independent experimental groups of plant extracts were resulted a perceptible rise in pH changes, while synergistically was not. pH increment might be due to released reactive oxygen species. Hence, Curcuma longa and Zingiber officinale plants might cause oxidative stress to induce apoptosis by increasing ROS activities or epigenetic regulations in independent experimental groups observed by pH changes.

Pediatric Hematology

PP-102
Role of CD117 in AML diagnostics in children

A. Palladına, O. Chernysheva, N. Kupryshına, N. Tupıtsyn
N. N. Blokhin NMRCO

Objective: CD117 is frequently expressed on blast cells in AML: 50–70% of cases are CD117-positive. CD117 is a transmembrane tyrosine kinase receptor encoded by c-kit oncogene. It is normally expressed on cells of many tissues including hemopoietic stem cells. CD117 binding of stem cell factor induces phosphorylation of CD117 and stimulates proliferation and survival of primitive hematopoietic stem cells. In normal bone marrow 2–4% of mononuclear cells and 25–50% of normal CD34+ bone marrow cells express CD117. The aim of our work was to prove that routine usage of anti-CD117 in immunophenotypic analysis of AML is necessary for further determination of minimal residual disease and also to assess the correlation between CD117 expression and FAB-variants of AML.
Methodology: Among 30 de novo AML patients, whose diagnoses were confirmed morphocytochemically and immunologically, there were these proportions according to FAB-variants: M0 (3 patients) M1 (6), M2 (4), M3 (3), M4 (2), M5a (3), M6 (2), M7 (8). Age of the children ranged from 0,5 to 18 years, with median of 3 years. CD117 expression on surface of the bone marrow blast cells was measured by flow cytometry.
Results: There were 30 patients, and CD117 was present in 73% of cases. The highest frequency of CD117 expression was found in M0, M4, M6 variants – 100% positive cases. In variants M5 and M7 there were 33% and 37.5% of positive cases, respectively. These results match the ones of other researchers. MRD after treatment was assessed in 17 cases, and positive expression of the antigen was stated in 4 of them (23%). Therefore, anti-CD117 may be useful in MRD studying in AML.
Conclusion: In AML there are still no special markers able to identify tumor cells in regenerating bone marrow. That's why establishing of CD117 expression status at diagnosis and knowledge of normal bone marrow cells expression profiles may help to access the MRD level after the induction treatment.

PP-103
Incidence of cytomegalovirus and Epstein–Barr infection after allogeneic bone marrow transplantation

G. Alakbarova, V. Huseynov, A. Mammadova, N. Aliyeva, R. Bayramli
Thalassemia Center of Baku

Objective: Viral infections, such as herpesviruses (CMV, EBV, HHV-6), adenovirus and polyomavirus, cause illness and lethargy due to major T cell malfunction in children with allogeneic hematopoietic cell transplantation (alloHCT). Cytomegalovirus interstitial pneumonitis (CMV-IP) is one of the most serious complications after alloHCT. The risk factors of CMV infection pretransplant time are known as follows, such as 1. unrelated donor marrow, 2. TBI, 3. anti-thymocyte globulin, 4. T cell depletion and 5. HLA mismatched donor. After transplantation period 1. acute GVHD and 2. use of steroid hormone are important risk factors. It is necessary to select an effective strategy for the prevention of CMV-IP after stem cell transplantation. Monitoring of Epstein-Barr (EBV) load is an appropriate approach to prevent post-transplant lymphoproliferative disease (PTLD) occurring after alloHCT.
Methodology: We conducted a retrospective study of pediatric patients undergoing alloHCT to investigate the incidence of and risk factors for CMV and EBV viremia and viral disease after alloHCT. This was a retrospective study of 26 pediatric patients who received alloHCT for malignant and nonmalignant diseases at the Thalassemia Center of Baku, Azerbaijan. Patients underwent transplantation between April 2018 and May 2019. Mean age range of these patients was <18 years. Our center created a standard operating procedure for prospective quantitative PCR monitoring for CMV and EBV. Patients were monitored at least once within 4 weeks before the start of conditioning regimen and then weekly for 180 days after alloHCT. CMV and EBV infection was evaluated by the CMV-DNA positivity shown by

the Real-Time polymerase chain reaction (PCR) method was performed as per protocol with QIAmp MinElute Virus Spin Kit and artus CMV and EBV RG PCR Kit (Qiagen, Germany) established using CFX-96 (BioRad, USA) analyzer. Negative result was CMV-DNA value >45 dpi/mL and EBV-DNA value >36 dpi/mL. The laboratory technique used was the commercially available qualitative enzyme chemiluminescent immunoassay (ECLIA) method using Cobas e411 analyzer with Elecsys Anti- CMV IgG assay kit (Roche Diagnostics, Mannheim, Germany) and EBV VCA IgM, EBV VCA IgG assay kit NovaLiSa (Novatec, İmmunodianostics, Germany) assay kit.

Results: Patients were considered to have viremia if CMV and EBV were >1,000 copies/mL on 2 consecutive PCRs respectively. After transplantation CMV DNA PCR was obtained positive in 8 (30.7%), EBV DNA PCR was obtained positive in 3 (11.5%) recipients. The incidence of multiple viremias, defined as PCR positivity for ≥2 viruses, was in 2 (7.6%) patients. CMV IgG was obtained positive in 12 (46%), EBV VCA IgG seropositivity was observed in 6 (23%) recipients before transplantation. In patients who are seropositive before transplantation, the incidence of CMV viremia approaches 70%.

Conclusion: Reactivation of latent herpesviruses results in outcomes ranging from asymptomatic shedding of viruses to severe diseases, depending on the immunological competence of the host. Severe and prolonged suppression of cellular and humoral immunity after alloHCT is accompanied by a high incidence of symptomatic recurrent herpes virus infections. Subclinical reactivation also occurs more frequently than previously expected in transplant recipients.

PP-104

Prevalence of thalassemia syndromes, hemoglobinopathies and mutation analysis in a tribal school in India

A. Oberoi, S. Kanakia
Lilavati Hospital and Research Centre, Mumbai

Objective: To detect the prevalence of Thalassemia Syndromes and Sickle Cell Anemia in a tribal school population of adolescent age group and Mutation Analysis of the positive cases.

Background: Thalassemia and other hemoglobinopathies are the most common monogenic disorders in India with a high prevalence in tribal populations. Social stigmas, difficult living terrains and high cost of treatment makes the management of such disorders difficult in the study population.

Methodology: This study was conducted on 211 children aged 10–14 years from a tribal school in the state of Maharashtra, India. After taking clinical history, complete hemogram report was obtained by an automated cell counter. High-performance liquid chromatography (HPLC) was performed on the samples with Bio Rad D-10™ Analyser. The samples with abnormal electrophoresis patterns were subjected to Next Generation Sequencing of HBH gene for mutation analysis.

Results: Of the 211 students sampled, 193 (91.5%) had a normal electrophoresis pattern and abnormalities were detected in 18 (8.5%) cases. β (beta) thalassemia trait was the commonest abnormality found in 16 (7.6%) children. Heterozygous Sickle Cell and Alpha Thalassemia were found in 1 (0.5%) case each. Of the 16 Thalassemia traits, 13 (81.25%) had IVS1-5(G>C) mutation, followed by c.47G>A (p. Trp16Ter) in 2 students (12.5%) and IVS1-1(G>T) c.92+1G>T in 1student (6.25%). The one sickle heterozygote had c.20A>T (p.Glu7Val) mutation.

Conclusion: High frequencies of these mutant alleles are maintained by the tribal populations probably due to consanguinity, lack of awareness and conveyance; low income status and high cost of treatment make them vulnerable. These groups must undergo premarital screening to decrease the risk bearing offspring with hemoglobinopathies.

PP-105

Monitoring serum ferritin overload in beta-thalassemia intermedia and major patients in Azerbaijan

D. Aliyeva, V. Huseynov, G. Alakbarova, R. Bayramli
Thalassemia Center of Baku

Objective: In β-thalassemia, major multiple blood transfusions may be a complication of iron overload in the body. This complication can impair the immune system, placing patients at greater risk of infection and illness. Routinely, iron overload can be monitoring by serum ferritin measuring. That is why in practice, it is used to monitoring chelation therapy in transfused patients. The aim of the present our study is to assess the serum ferritin levels in multi-transfused β-thalassemia major and intermedia patients. The study was also done to estimate the present situation of iron overload in them.

Methodology: During 5 months (between May to September 2018) 1640 samples with clinically diagnosed β-thalassemia intermedia and major patients we screened for their serum ferritin measuring at Thalassemia Center of Baku, Azerbaijan. Serum ferritin measured by electro-chemiluminescence (ECLIA) method using a Cobas-e411 Analyzer. Data were analyzed to determine the association between variables serum ferritin levels. The association between age, sex, and serum ferritin level were established.

Results: In our study, we searched serum ferritin 450 (27.4%) 1,000 ng/mL, 819 (49.9%) between 1,000 to 2,500 ng/ml, 216 (13.2%) above 2,500 ng/ml, 77 (4.69%) between 4,001 to 5,500 ng/mL and 43 (2.6%) 5,501 to 7,000 ng/mL. In our study serum ferritin levels above 7,000 ng/mL was 35 (2.13%). Age of patients was 1–58 years, among them 874 (53.3%) men and 766 (46.7%) woman. These levels reflect insufficient chelation therapy and to develop iron overload related complications.

Conclusion: Transfusion dependent thalassemic patients with a high level of serum ferritin recorded in this study give the rationale for regular screening with respect to iron overload to ensure proper management of iron overload associated complications. Right chelation therapy could improve the quality of life of these patients.

PP-106

Parvovirus B19 induced posterior reversible encephalopathy syndrome in a patient with relapse acute lymphoblastic leukemia

H. Sarbay[1], T. Atay[2], A. Atay[1], B. Malbora[1], F. Garip Uçar[3], T. Atasever Rezanko[4], N. Bakar[5]
[1]TC Yeni Yuzyil University Faculty of Medicine Pediatric Hematology and Oncology; [2]TC Yeni Yuzyil University Faculty of Medicine Pediatrics; [3]TC Yeni Yuzyil University Faculty of Medicine Dermatology; [4]TC Yeni Yuzyil University Faculty of Medicine Pathology; [5]TC Yeni Yuzyil University Faculty of Medicine Radiology

Background: Human parvovirus B19 (B19) is a small, single-stranded DNA virus that binds the cellular receptor P antigen on erythrocytes. Complications from parvovirus B19 infection are common in children during chemotherapy for hematologic malignancies, including acute lymphoblastic leukemia (ALL). Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological syndrome characterized by symptoms including a headache, seizures, altered consciousness and visual disturbances. It is commonly associated with acute hypertension. Recent reports reveal that PRES can be associated with B19 infection. In this report, we present a case of PRES induced by Parvovirus infection in a patient with relapsed ALL.

Case report: A 9-year-old male patient who was treated with B cell ALL between 2015 to 2018 was hospitalized with the diagnosis of early relapse combined with bone marrow and testis 8 months after the end of treatment. Bone marrow aspiration showed diffuse L1-L2 type blast, and testicular ultrasound was consistent with leukemic infiltration in the left testis. Left orchiectomy and biopsy of the contralateral testis were performed. The ALLIC-BFM relapse 2016 protocol was initiated. Subfebrile fever occurred on the 3rd day after chemotherapy in the 4th week of treatment. The patient had no signs other than mild serous nasal discharge, and abdominal pain started 2 days later. Two days later, the patient had first plunge and then right-sided tonic-clonic convulsions. Antiepileptic treatment was started with midazolam,

phenytoin and levetiracetam. Lumbar puncture could not be performed due to recurrence of intermittent convulsions due to unstable general condition of the patient. Fever ranged from 37 to 38.5 °C and arterial blood pressure was 95 percentile for age. Empiric antibacterial and antiviral therapy was initiated because of inability to rule out central nervous system infections. Laboratory results revealed white blood cell: 0.22×10^9/L, hemoglobin: 8.3 g/dL, platelet: 37×10^9L, glucose: 108 mg/dl, urea: 14 mg/dL, creatinine: 0.35 mg/dL, AST: 32 IU/L, ALT: 76 IU/L, Na: 133 mmol/L, K: 4.4 mmol/L, Ca: 8.6 mg/dL, Cl: 95 mmol/L, Mg: 1.9 mg/dL. Intravenous magnesium supplementation was started to maintain anti-hypertension and magnesium levels above 2 mg/dL. Cranial magnetic resonance imaging showed no signs of bleeding or leukemic involvement in favor of thrombosis. Diffusion restriction in diffusion-weighted imaging and no significant pathological contrast enhancement was detected in postcontrast examinations. His convulsions were controlled within 2 days, and neurological findings and unconsciousness regressed within 4 days. Ten days later, itchy macular rash developed on the trunk and extremities. HSV type I-II IgM, Rubella IgM, EBV-CMV DNA PCR tests were negative and Parvovirus DNA PCR test was positive (580 IU/ml, 1 copy 1.43 IU). PRESS induced by parvovirus infection was considered. The rash disappeared spontaneously within 4 days. Antibacterial and antiviral treatment was completed to 14 days. The patient is being followed up.

Conclusion: In conclusion, parvovirus infections may cause serious complications in immunosuppressive patients. PRES is a common condition especially in patients with acute leukemia and bone marrow transplantation. Early initiation of supportive treatment is important to prevent serious complications.

PP-107
Patients with thalassemia major receiving hemotransfusion: specifications of chelation therapy depending on ferritin level

V. Huseynov, S. Jalilova, N. Verdiyeva, R. Bayramli, A. Nasibova
Baku Thalassemia Center

Background: Thalassemia is a common hereditary disease in the world and in our country. In thalassemia patients iron overload occurs due to frequent hemotransfusion and increased iron absorption from in the gastrointestinal tract. The main cause of iron overload in patients with transfusion dependent thalassemia is blood transfusion. The aim of Chelation therapy is to prevent iron overload in the body, reduce existing iron deposition, and thus prevent complications caused by iron load. That is why, chelation therapy should be started before iron overload occurs and iron level must be maintained. Currently used chelating medicines are desferroxamine (DFO), deferasirox (DFX) and deferopirone (DFP).

Methodology: Cases of 1,003 patients with dispensary registration and receiving chelating therapy in the Thalassemia Center during 2009–2019 years were evaluated retrospectively. Assessments included HB electrophoresis, age group, physical examination (splenomegaly, hepatomegaly, asplenism), quantity of hemotransfusions per year, serum ferritin level, transplant status, mono and combined chelate treatment, liver-kidney functional tests, viral serological tests (HbsAg, Anti HCV), adverse effects of the chelators.

Results: 1,003 patients with age group 3–43 years received chelation therapy, where 993 patients with thalassemia major received hemotransfusion (h/t), and 10 patients received chelation therapy after bone marrow transplantation. These patients received a hemotransfusion of about 2–4 weeks, approximately 15–35 times a year. Thalassemia patients were divided into two groups: monotherapy and combination therapy groups. Each group also divided into 3 subgroups. DFO, DFP, DFX monotherapy, DFO+DFP, DFP+DFX, DFO+DFX combination treatment. In each group, the number of patients, the lowest and highest levels of ferritin was assessed. The number of patients in the monotherapy group was more in DFO (327 patients) and DFX (233 patients) groups than in DFP (148 patients) group. These two groups(DFO and DFX) patients were similar in number. The number of patients receiving in DFO+DFP in combined groups (222 patients) were more than in DFO+DFX (57 patients) and in DFP+DFX (78 patients) combined groups. There was little difference between the number of patients in the other two groups. The patients used both monotherapy and combined therapy without being suspended from the ferritin level. The group receiving DFO were usually elder patients and older patients(age of patients 17–43). DFX was started in initial chelate therapies. The younger age group was more common. The age limit in the combined treatment areas yielded different results. As a result, ferritin level is not sufficient criteria to start chelators, patients characteristics, transfusion number, drug compliance, drug access and most importantly, iron accumulation in organs should be examined.

Conclusion: Continuous hemotransfusion and chelate therapy have increased the quality of life in thalassemia patients. Detection of complications in thalassemia patients with hemotransfusion in time will facilitate our work in terms of treatment and follow-up. In chelation therapy, sometimes monotherapy is not enough to reach any target. At this time, you need to increase the dose, change the drug, or apply combination therapy.

PP-108
Specifications of chelation therapy in patients with thalassemia intermedia and other thalassemia disorders

S. Jalilova, Z. Mirzayeva, X. Jafarova, Z. Mammadbayov, V. Huseynov
Baku Thalassemia Center

Objective: Iron overload occur in non transfusion depending thalassemia including beta thalassemia intermedia, HbH disease and other thalassemia syndromes due to increased iron absorption from the intestines and random transfusion. In patients with thalassemia intermedia, iron is mostly accumulated in liver and endocrine organs. Requirements for starting therapy and treatment maintaining are more different in patients with thalassemia major than those with thalassemia intermedia.

Methodology: Cases of 42 patients with dispensary registration who received chelation therapy in the Thalassemia Center during 2009–2019 years were evaluated retrospectively. Provided assessment included Hb electrophoresis test, age group, physical examination (splenomegaly, hepatomegaly, asplenism), quantity of hemotransfusion received per year, hydrea intake, serum ferritin levels, chelation therapy, kidney and liver functional tests, viral serological tests (HbsAg, Anti HCV).

Results: The majority of patients between 8–57 years (in total 42 patients) age group receiving chelation therapy had beta thalassemia intermedia whereas remaining patients had other thalassemia disorders(69% thalassemia intermedia, 19% HbH DISEASE, 9.52% HbE/beta thalassemia, 2/38% HbE/alpha thalassemia. These patients were divided into 2 groups: patients receiving few hemotransfusions (h/t) and patients who never received hemotransfusion. Patients receiving chelation therapy as a monotherapy were divided into three semi-groups: Desferroxamine (DFO), Deferipron (DFP), Deferasirox (DFX) monotherapy semi-groups. Each group assesses for the number of patients and for the lowest and highest ferritin levels. Ferritin levels were higher in patients who did not receive transfusion compared to the patients who are transfusion dependent. Max ferritin level in non-depending thalassemia intermedia was 3,920 ng/ml, but in transfusion depending thalassemia intermedia 1,125 ng/ml. This is the main reason for the accumulation of iron in this group of patients by increased gastrointestinal absorption. The number of patients receiving chelators was more in the DFX group. 14patients of 23 patients received DFX. As in thalassemia intermedia iron accumulation occurs more frequently in the liver and DFX is better for liver iron deposition.

Conclusion: Even if patients with thalassemia intermedia does not receive transfusion, or receive it randomly, accumulated iron may cause lung hypertension, hypothyroidism, hypogonadism, and osteoporosis. Therefore, chelation therapy should be considered in these patients as in patients with thalassemia major. The level of ferritin may be a criterion for initiating therapy in cases of liver MRI absence. Concentration of iron in liver tissue assessed by biopsy is golden standard for measuring iron overload in the body of such patients. Iron concentration and serum ferritin level should be evaluated once a year and in every 3 months, respectively in patients starting from 10 years old. LIC >5 mg Fe/g; and serum ferritin >800 ng/ml is the indication of chelation therapy. Chelation therapy should be stopped if iron level reduction below 3 mg Fe/g or ferritin level less than 300 ng/ml in dry liver tissue observed.

PP-109

Isolated optic nerve and cerebral involvement without cerebrospinal fluid lymphoblastocytosis as a presenting sign of relapsed pediatric acute lymphoblastic leukemia

N. Karakurt, C. Albayrak, Ü. Özgen
Ondokuz Mayis University, School of Medicine, Department of Pediatrics, Division of Hematology

Case report: Central nervous system (CNS) chloroma is extremely rare presentation of CNS relapse in acute lymphoblastic leukemia (ALL). We report a Philadelphia chromosome-positive (Ph+) ALL patient who had isolated optic nerve relapse without blasts in cerebrospinal fluid (CSF), after hematopoietic stem cell transplantation (HSCT), and outline a treatment plan of systemic chemotherapy and CNS directed therapy. Sixteen-year-old boy was diagnosed with Ph+ ALL and induction therapy on ALL IC 2009 protocol with imatinib mesilate was started. He did not have any neurological impairment nor leukemic blasts in CSF at time of diagnosis. He was noted to achieve remission after the induction therapy. Prophylactic radiotherapy was not applied. HSCT from full matched sibling donor was performed eight months after the initial diagnosis. Total body irradiation (TBI) was not available. Chimerism of 92% was observed in third and sixth months after HSCT. At 9th month after HSCT, he presented with acute onset pain in right eye, followed by loss of vision. Bone marrow aspiration and CSF evaluation was negative for leukemic blasts. Fluorescein fundus angiography showed vascular occlusion at the level of optic nerve. Cranial and orbital MRI showed increased contrast uptake in optic nerves, predominantly in the right side. He was diagnosed with isolated optic nerve relapse. He subsequently received weekly/twice weekly triple intra-thecal therapies (methotrexate, cytosine arabinoside and prednisone) followed by local radiotherapy. He was also given systemic high-risk arm chemotherapy according to ALL-IC study group, 2016, childhood ALL 1st relapse guidance. Bone marrow relapse was not observed and CSF was negative for leukemic blasts during repetitive intrathecal therapies. On the second week of induction therapy, three months after the time of relapse, the patient developed acute onset loss of conscious and right hemiparesis. MRI showed abnormal diffusion restriction and increased contrast uptake in left cortical gyri in neighbourhood of central sulcus, which was compatible with leukemic infiltration. He died due to progressive central nervous system disease. Generally, CNS disease is diagnosed by microscopic analysis of CSF with presence of leukemic blasts. However, clinical or radiological signs without leukemic cells in the CSF, which is deeply rare is also defined as CNS disease. A recent study from Nordic Leukemia registry demonstrated that 3.5% of patients with ALL had CNS involvement in ALL and among those with CNS disease, only 9% presented with CNS symptoms without blasts in CSF. Heath et al reported two pediatric patients with CNS relapse (chloroma with CSF lymphoblastocytosis). Kraal et al. also reported a two-year-old ALL patient with optic nerve involvement accompanying blasts in CSF. However, Ph+ ALL with isolated CNS relapse without blasts in CSF has not been reported. A review of the literature indicates that multiagent chemotherapy combined with CNS therapy may be effective, with/without HSCT. Our patient had progressive disease and refractory to all therapies applied. We suggest that, in order to prevent CNS relapses, the use of prophylactic radiotherapy may be a cornerstone in developing countries where TBI is not available.

PP-110

Relationship between liver iron concentration determined by liver MRI (SIR method) serum ferritin and liver enzymes in patients with thalassemia major

V. Huseynov, N. Verdıyeva, R. Bayramlı
Baku Thalassemia Center

Background: Thalassemia is the most common hereditary disease. Chronic blood transfusion is the mainstay treatment of patients with thalassemia major. Which causes iron overload in some organs (liver, heart, endocrine glands.). This is the main complication of hemotransfusion.

Aim: This study aimed to explore the degree of iron overload in liver, using relationship with serum ferritin level, liver enzymes (ALT, AST) and hepatic MRI (SIR method).

Methodology: In this study we selected 65 patients with transfusion dependent thalassemia major (TDT) followed in Thalassemia Center of Azerbaijan who had been evaluated by liver MRI (SIR method) in Caspian International Hospital between February 2018 to October 2018.

Results: Patients included in the study are 6–37 years old and receive hemotransfusion every 2–4 weeks. All patients are classified into three groups based on the degree of iron load in the liver: bland iron loading (50–150 μmol/qr), middle iron loading (125–270 μmol/qr), severe iron loading (>270 μmol/qr). Only two patients had liver iron load normally (<50 μmol/qr). The liver enzymes in these patients were normally, and serum ferritin was <500 ng/ml. Liver enzymes of patients with bland iron load in the liver were found in normal range, serum ferritin in 5 patients values in the range from 300 to 1200 ng/ml, in one patient was >2,000 ng/ml. Liver enzymes In 8 patients with middle iron load in the liver were found in normal range, only in 1 patient ALT was 55 U/L, serum ferritin values in the range from 500 to 3,100 ng/ml. Liver enzymes in 20 patients with severe iron load in the liver were found in normal range, in 28 patients ALT was high than normal range (31–196 U/L), serum ferritin values in the range from 728 to 10,566 ng/ml. In all patients, results of viral serological tests were normally. We found a statistically significant relationship between serum ferritin, liver enzymes and liver MRI. Serum ferritin and liver enzymes were lower in patient with bland and middle iron load than in patients with severe iron load.

Conclusion: In patients with thalassemia major who receive hemotransfusion, liver iron load should be properly evaluated as a serious complication. Hepatic iron deposition rises with increasing age. Liver MRI (SIR method) is one of the main examination methods. We recommend measuring liver iron load once a year with MRI and evaluate the result together with serum ferritin and liver enzymes.

PP-111

Chimerism after stem cell transplantation for thalassemia patients

N. Alieva, A. Nasibova, P. Safarova, S. Sultanova
Center of Thalassemia

Objective: Allogeneic hematopoietic stem cell transplantation (Allo-HSCT) is the only curative treatment option for thalassemia patients. The objective of the transplant procedure in these diseases is to achieve stable and durable engraftment to improve the hematopoietic function. Complete donor haematopoiesis not essential for sustained engraftment and the simultaneous presence of haematopoietic cells of both donor and recipient origin is not rare event after HSCT in these patients. Persistent mixed chimerism after Allo-HSCT may result cure for thalassemia major patients. But mixed chimerism (MC) may be associated with rejection. We report the outcome in 38 HSCTs for thalassemia patients were reviewed retrospectively, who had successful engraftment and had more than 2 years follow-up.

Methodology: Between May2014 and December 2017, 38 patients had received an allogeneic HSCT for β-TM in our Center were included in this study. Chimerism was detected by fluorescence in situ hybridization (FISH) or short tandem repeats (STR).

Results: Chimerism was first assessed at day +25–30, then every 2–3–12 months or more frequently if there was MC. If the rejection was suspected, immunosuppression was stopped and donor-lymphocyte infusion (DLI) was given if there was no response. The median age of the patients was 7 years (range 2–18), 13/38 (34.2%) complete chimerism (CC), 25/38 (65.8%) mixed chimerism at day +30. MC was quantified at level 1 (residual host chimerism (RHC) <10%) in 8 (32%), level II (RHC 10–25%) in 4 (16%) and level III (RHC >25%) in 13 (52%). DLI was administered to 4/25 (16%), from them 2 evolved to MC, 2 rejected the graft. At the end of the first year: 14/38 (36.8%) had CC, 17/38 (44.7%) had persistent MC, 7/38 (18.4%) rejected the graft. 5/7 graft rejected patient had level III MC.

Conclusion: Persistent mixed chimerism can result cure for beta-thalassemia patients after HSCT. But our study confirmed that the presence of large amounts of residual host cells (RHC >25%) within the first 3 months after

transplantation is a risk factor for graft rejection. This report describes a large series of patients with MC post HSCT for beta thalassemia with long-term follow-up.

PP-112

Treatment approach to thalassemia patients with alloimmunization at the Baku Thalassemia Center

K. Bagirova, S. Hasanova, G. Memmedova, V. Hüseynov, R. Bayramlı, P. Abbasova
Thalassemia Center Baku, Azerbaijan

Objective: Beta thalassemia is the most common congenital hemolytic anemia in Azerbaijan. Cardiac, endocrine, iron overloading and allo/autoimmunization create the possible complications in treatment among patients with transfusion dependence. Alloimmunization increases the need for patients' transfusion, negatively affects the quality of life. In this study, we evaluated our treatment approach to thalassemia patients who have received treatment at our center and whose DAT test is positive and transfusion response was decrease.
Methodology: The study included 18 patients (Beta Th. major n=14 (77.7%) Beta Th. intermedia n=4 (22.2%) with DAT (n=18, 100%), IDAT (n=14, 77.7%) positivity, increased transfusion requirement and severe hemolysis the previous year in Baku Thalassemia Center. Patients with significant clinical signs and positive DAT test were accepted as alloimmunization and thus appropriate treatment was decided to be started. Patients were started with steroid dose of 1mg/kg/day and steroid pulse therapy, IVIG, immunosuppressor, therapeutic apheresis. immunosuppressor was used as calcineurin inhibitor Cyclosporin in dose 1–6 mg /kg/day.
Results: There were 18 patients including in the study. Among them are 11 males (61.1%), 7 females (38.8%) and male: female ratio was 1.57:1. 8 of patients (44.4%) received 1 mg/kg/day steroid treatment only and 9 (50%) steroid pulse therapy benefited. Total 6 patients (33.3%) were given per os cyclosporin treatment, 4 patients (22.2%) were given cyclosporin + IVIG treatment and 2 (11.1%) patients received CSA+IVIG+therapeutic apheresis. Although the diagnosis of 3 patients was known from their childhood, they did not receive transfusion therapy consciously. At the time of hospitalization their Hb was 2.5–4 g/dl. Since DAT was positive in these patients, steroid therapy was started, but no response to low dose steroid and pulse therapy and CSA were initiated. One of primary patients of 7 years old with anemia detected was diagnosed Beta Thalassemia intermedia and HCV. As this patient has DAT positivity and no transfusion response, steroid therapy was initiated. The response to therapy was determined by the reduction of clinical symptoms (signs of hemolysis) and the need for transfusion. Although 11 patients (61.1%) had no clinical symptoms, DAT was positive for a long time. Patients receiving transfusions once a week after treatment decreased the need for transfusions up to 1 transfusion per month.
Conclusion: Although the major and minor groups (C, c, E, e, Kell), cross match suitable, cleaned and irradiated erythrocytes are transfused to thalassemia patients in our center, alloimmunization is a common complication. Antigen-negative transfusion is recommended for alloimmunised patients. At present time the antibody screening and identification tests are not done in our center, so this study is related on DAT test, and so we cannot give antigen negative transfusions to our alloimmunised patients. In order to manage with these patients better, antibody screening and identification tests are planned in our center in brief time. In these cases, the number of patients who do not respond to the first step steroid therapy is sufficient. Therapeutic apheresis, cyclosporine and other immunosuppressor drugs and antigen negative transfusions must early and widely used in the treatment among these patients.

PP-113

Consolidation treatment with high-dose chemotherapy and radiotherapy in children and young adults with relapsed and refractory Hodgkin's disease

N. Subbotina, E. Belyaeva, I. Dolgopolov, A. Popa, V. Boyarshinov, V. Daylidite, G. Mentkevich
Blokhin's National Medical Research oncology center

Objective: Treatment of relapsed and refractory Hodgkin's lymphoma of children and young adults is an actual problem for oncologists worldwide. The outcomes for these heterogeneous group of patients are different and depend of the volume of previous treatment, time to relapse, chemoresistance of the tumor, etc. The greatest therapeutic challenge is dealing with the refractory disease. High dose chemotherapy with autologous HSCT is routinely used to improve treatment results for such pts. Radiotherapy may help to overcome tumor resistance to HDCT.
Methodology: Data of 36 pts with refractory (n=14, 39%) and relapsed (n=22, 61%) HL were analyzed. The median pts' age was 16 (4–20) years. All pts was treated with induction CT ICE (n=12, 33%), ViGePP (n=17, 47%), ICE changed to ViGePP in non-responders (n=6, 17%) or ViGePP to ICE (n=1, 3%). Consolidation included radiotherapy and HDCT with autologous HSCT. In 12 pts with refractory disease we used "up-front radiotherapy" immediately before HDCT. Doses of "up-front radiotherapy" varied from 10 to 22.5 Gy according to the treatment zone and previous irradiation. In case of lymphoma spreading both sides of diaphragm "up-front" irradiation was given to the "upper part" followed by HDCT and radiotherapy continuation to the rest of the tumor.
Results: HDCT consisted of ARA-C 4000/Mel 140 (n=22, 61%), or VP-16 1400/Mel 140 (n=7, 19.5%), or Benda160/Mel 140 (the latest group, n=7, 19.5%). The graft source was PBSC in 17 (47%), BM in 6 (17%), PBSC + BM in 13 (36%) pts. The regimen toxicity was < st.3 in 29 (80.5%) pts, st.3 in 7 (19.5%) pts. The less toxic was Benda-Mel regimen: no toxicity > st.2. The strategy of "up-front radiotherapy" didn't increase toxicity of HDCT. Median time of WBC recovery was 14 (10–21) days. From 9 pts (25%) who relapsed/progressed after HDCT 6 (17%) died of DP and 3 got the next line treatment (1st is being in CR and well for 5 years). At all 27 pts (75%) are alive in remission with a median follow-up 105 (1–189) months, 2 (5%) died of infection and toxicity on next line treatment and 1 pt (3%) was lost of follow-up. The 5-year OS probability in all group was 76.8±7.7%; 5-year EFS 74.2±7.9%. For chemo sensitive relapses (n=8), primary refractory (n=14) and refractory relapses (n=14) 5-year OS probability was 100%, 75.0±12.7% and 58.7±14,.2%, respectively, p=0.2; 5-year probability of relapse 0%, 28.7±14.1% and 34.7±14.2%, respectively, p=0.2.
Conclusion: Therapeutic programs including HDCT was successful in all our pts with chemo sensitive relapses of HL. For pts with refractory disease concomitant use of radiotherapy and HDCT in consolidation provided up to 75% of long-term survival. Toxicity of HDCT regimens was mild even with "up-front radiotherapy". For some pts with refractory disease additional approaches are needed to improve survival.

PP-114

Treatment approach and results of therapy relapse/refractory patients with acute lymphoblastic leukemia in Talassemia Center Baku

G. Mammadova, K. Bagirova, S. Hasanova, P. Safarova, R. Bayramlı, A. Nasibova, V. Huseynov
Thalassemia Center Baku, Azerbaijan

Objective: Acute lymphoblastic leukemia (ALL) is 75% of all leukemia that are common in children. The most common cause of failure in ALL treatment in children is relapsed (~15–20%). The treatment of the primary ALL children in Azerbaijan is underway of Moscow-Berlin (MB) and BFM protocols. The purpose of this study is investigation of the effects and the results of chemotherapy (CT) protocols in our center.
Methodology: The prospective study included 20 relapse/refractory ALL diagnosed, who received antirelapse CT in Thalassemia Center from 2014–2019. 17(85%) of the patients were male, and 3(15%) were female. 19 (95%) patients were diagnosed B-cell leukemia (n=7 pre-B, n=12 B-common) and 1 (5%) patient were T cell leukemia. Patients including in the study were divided

into the following age groups: 0–4 years – 3 (15%) patients; 5–9 years – 9 (45%) patients; 10–14 years – 6 (30%) patients; 15–17 years – 2 (10%) patients. Isolated bone marrow relapsed (BM) were in 17 patients (85%), extramedular (CNS, testicular) + BM combined relapse was recorded in 2(10%) patients, isolated testicular relapse was in1 patient (5%). 18 of these patients received the CT MB protocol but 1 patient got the MB protocol.

Results: 19 (95%)of the patients including in the study, initially received the ALL REZ BFM-2002 protocol, and 1 patient got IDA-FLAG on 1st line CT. During the 1st anti-relapse CT has been achieved remission at 12 (60%) patients, 4 (20%) patients were refracted, 3 (15%) patients died from multi organ failure and 1 patient (5%) was expected to be treated. All of the refractory patients are patients who received CT on the ALL REZ BFM-2002 protocol. Patients with refractory disease were treated with FLAG-IDA, basing on NELARABIN, EMA protocols. 1 (5%) of refractory patients has been achieved remission after 2nd CT line but this patient was relapsed after HSCT and other 3 patients died of multiorgan failure during CT. Total number of patients in complete remission after 2nd line CT was 13(65%). 8 (40%) of the patients after the complete remission were underwent HSCT, where 3 (15%) of the patients were second relapsed and then died, 1 (5%) was relapsed and continued his CT, and 4 (20%) are in remission at present time. 9 patients (45%), included in the study, died at different stages of treatment. This group was between 8 and 16 years of age. Among 13 (65%) patients who had remission, 6 of them (30%) the 1st relapse time is more than 20 months. The total 12 months survival is 25% (n=5).

Conclusion: The patients who got remission are made HSCT after ending the chemical therapy. Patients who were not made HSCT did not have the matched donor. Taking into account that relapse/refractor ALL is difficult in treatment, thus, there is a need to improve treatment protocols. Our center is planning to use widely these protocols and targeted drugs of new generation.

PP-115
Extended half-life product (rFVIIIFC) for treatment of children with hemophilia A: preliminary post-switch experience from a tertiary care center

M. Alsaleh, T. Owaidah, H. Khalil, H. Alzahrani, A. Aljefri, B. Safi, V. Mohammed
King Faisal Specialist Hospital & Research Centre, Riyadh

Objective: Factor VIII replacement therapy is standard of care in Hemophilia A (HA) patients to prevent or reduce morbidity arising from joints and muscles bleeds. Extended half-life (EHL) product, factor VIII fc fusion (rFVIIIFc) was introduced into the comprehensive hemophilia care program of Pediatric Hematology/Oncology department at King Faisal Specialist Hospital and Research Centre, Riyadh, a leading tertiary referral center for inherited clotting factor deficiencies in the Kingdom

Methodology: To summarize experience with rFVIIIFc protein in Saudi children during the initial twenty months of the drug's availability, data was collected from Hemophilia Patient Management system, designed on REDCap (Research Electronic Data Capture) application.

Results: Factor VIII Fc fusion protein, Eloctate approved for use in children with HA was included on institutional formulary on November 25th, 2017; total of 58 children (≤14 years) were switched from Standard Half-life product to Eloctate and a median age of 8.4 years (0.6–14 years) observed. Co-morbidities prior to switch observed in 36% (21): haemophilic arthropathy, 21% (12); Intra-cranial hemorrhage, 9% (5) and others, 7% (4). Prophylactic treatment observed in 76% (34) pre-switch, with all patients currently on prophylaxis. Lesser infusions were the main (80%) reason to switch followed by latest technology (20%) available. Early short quality-of-life (QoL) survey revealed majority (>90%) were satisfied with lesser infusions and early resolution of their bleeding symptoms, longer follow-up QoL surveillance is warranted.

Conclusion: In our experience patients and families are aware and keen on adapting EHL products in their management plan, preliminary survey suggests better QoL post-switch. We have initiated a real-world observational study in-line with the ASPIRE study while WAPPS-Hemo system participation will enable pharmacokinetics evaluations of the same. Additionally, EHL product (rFXII) Alprolix was recently approved to be included on the institutional formulary for the management of Hemophilia B (HB) patients and a plan to join the international chart review study entitled B-MORE study is underway. Participation on the aforementioned real-world data collection studies would enable clinical data unique to this region, while a longer follow-up would enable cost-effectiveness analysis assisting other countries in the region planning to integrate EHL in respective hemophilia care programs.

PP-116
Autoantibodies associated with major thalassemia

A. Amına, G. Sabıha, M. Hacene
Badji Mokhtar University Medecine Faculty, University Hospital Center, Annaba, Algeria

Objective: β-thalassemia is an autosomal recessive disorder common worldwide. The major form of β-thalassemia, or Cooley's disease, is manifested by severe anemia in early childhood: it is symptomatic only after several months of life. Many thalassemic patients have chronic liver disease, the two main causes being iron overload and HCV infection. The aim of this study is to report the auto-Ac profiles of 18 patients with β-thalassemia major.

Methodology: 18 sera of patients with β-thalassemia major (12 women and 06 men with a mean age of 24 years), all patients were referred for suspicion of autoimmune hepatitis (hepatic cytolysis, jaundice, splenomegaly, cholestasis) with serology negative viral (HCV, HBV). The immunoassay carried out concerned the search for anti-nuclear antibodies (ANA) and the search for non-organ specific anti-tissue antibodies.

Results: The ANA search was positive for 56.25% of the sera and revealed a heterogeneity of autoantibodies as follows: 43.75% were speckled and 12.5% nucleolar in appearance. 43.75% of the sera are negative in ANA. Regarding the search for ANSO was positive for 77.78% of which: 72.22% are anti-smooth muscle (anti-ML) and 5.55% are anti-mitochondrion type 2 (AMA2). 22.22% of the sera are negative in non-organ specific anti-tissue antibodies.

Conclusion: β-thalassemia is a public health problem because of its number and severity. The clinical and biological disorders they cause are responsible for the disruption of biochemical and immunological parameters.

PP-117
Hemophagocytic lymphohistiocytosis: a case series of a Libyan institution

A. Malek[1], M. Eddeb[2], F. Alrıanı[3], M. Benabdullah[4], H. Ahmed[5]
[1]Emitiga Hospital; [2]Tripoli Medical Centre; [3]Tripoli Children Hospital; [4]Tripoli Central Hospital; [5]Tripoli University

Objective: To describe the clinical and laboratory presentation of hemophagocytic lymphohistocytosis in children treated at Tripoli children hospital.

Methodology: 12 cases of HLH are in the study, their age was between 1.5 to 36 months, male to female ratio was 1:2. This is a retrospective descriptive study of cases of hemophagocytic lymphohistiocytosis (HLH) in pediatric age group which was conducted in Tripoli children hospital, hematology and oncology department, Libya.The data were collected from the archive between 2012–2019, which included the clinical presentation, investigations and follow up data up to discharge.

Results: Hemophagoycytic lymphohistocytosis (HLH) is a rare, aggressive and life-threatening which is caused by overactivation and accumulation of macrophages (Histocytes) and Lymphocytes. The disease is most common seen in infants and young children but it might affect adults of any age. All the cases in the study presented with fever in which their temperature was between 38 to 40, and mean temperature of 39.41±0.63. Regarding their physical examination, 5 patients presented with rash, 10 presented with hepatosplenomegaly associated with ascites, and one patient presented with an isolated splenomegaly. 4 patients presented with jaundice, neurological symptoms and lymphadenopathy, 3 of them presented renal impairment; however, half of them presented with respiratory symptoms. From their social history, 50% has a positive family history of the same illness, also about 66.6% their parents were in consanguinity. In regard to their lab investigations. All cases were anemic, 41% showed leucopenia, 25% leukocytosis, 91%

thrombocytopenia. hypertriglyceridemia was in 83% of them, and D-dimer was positive in 50% of the patients. 3 of them revealed that their fibrinogen was high, ferritin >500 ng was in 10 of them; however, ferritin >3,000 ng was in only 3 of them. The immune marker sCD 25 titer was elevated in 87.5%, and bone marrow biopsy showed that there was an evidence of heamophagocytosis in 50% of the cases. The HLH disease was a primary in half of them; however,the other half were associated with underlying immune and hematological disorders such as, acute lymphoid leukemia, Chediak Haigashi syndrome, Epstein Barr virus, Omenn syndrome, severe combined immune deficiency (SCID). Finally, according to their treatment, all of them had received dexamethasone, platelets, and blood transfusion. 9 of them received cyclosporine, 2 patients had received intrathecal methotrexate as part of their treatment. A bone marrow was done in Jordan for only 1 patient, and fortunately the patient survived. Only 3 of the cases have survived.

Conclusion: As reported before, HLH has a multifaceted presentation with non-specific features. It may be treated with immunochemotherapy; however, the bone marrow transplantation is fundamental for its cure. A further study should be done in the field of its treatment in Libya.

PP-118

Chemotherapy-induced rhabdomyolysis in chidren with leukemia: a case report

S. Vural[1], S. Karaman[2], S. Yilmaz[3], G. Sumlu Ozcelik[4], N. Akinci[4]
[1]University of Health Sciences Istanbul Sariyer Hamidiye Etfal Education and Research Hospital, Department of Pediatric Hematology-Oncology; [2]Istanbul University Istanbul Faculty of Medicine, Department of Pediatric Hematology-Oncology; [3]Dokuz Eylül University Medical Faculty,Pediatric Hematology Department; [4]University of Health Sciences Istanbul Sariyer Hamidiye Etfal Education and Research Hospital, Department of Nephrology

Background: The rhabdomyolysis (RML) is the result of the release of the cell contents into the serum after injury of the skeletal muscle and may occur due to various reasons. In patients with cancer, rhabdomyolysis cases have been reported rarely after chemotherapy. In this paper, we present a case of acute lymphoblastic lymphoma who developed severe liver dysfunction and diagnosed as rhabdomyolysis during the febrile neutropenia attack.

Case report: 10-year-old male patient with a history of recurrent lymphoblastic lymphoma was admitted to our hospital with a painful swelling of the left lower back of his left arm and back three days after the first block of the chemotherapy (ALLREZ BFM 2000). She had a feverish appearance and had a oral mucositis and 38°C fever. The left arm medial 10×10 cm, left lumbar paraspinal region 20×10 cm, unclear borders, painless soft tissue swelling was found. Laboratory findings were revealed pancytopenia, elevated transaminase and hyponatremia. Piperacillin-tazobactam and teicoplanin were started for febrile neutropenia. After a few hours, a 15×15 cm swelling developed in his right calf. Ultrasonography and magnetic resonance imaging revealed intramuscular hematoma. Coagulopathy was present but no inhibitors detected against to coagulation factors. When urine was dark red, the desired creatinine kinase (1,481 U/L), LDH (1,305 U/L) and urine myoglobin (644 ng/mL) were found to be high. She was started on hydration with the diagnosis of rhabdomyolysis. In the follow-up, total bilirubin levels were decreased to 19 mg/dL, indirect bilirubin to 10 mg/dL and creatinine kinase to 5,100 U/L. The findings regressed with antibiotic and supportive treatments. All cultures were sterile. During the two-week period, all examination and laboratory results were improved, and the patient completed the chemotherapy protocol without any problem

Conclusion: In all clinical conditions such as sepsis, muscle pain, if dark urine is present, rhabdomyolysis should be considered, and early diagnosis and treatment can prevent life-threatening.

PP-119

Congenital factor XIII deficiency with the presence of inhibitor: a case report

S. Karaman[1], A. Unuvar[1], D. Tugcu[1], F. Bilgili[2], S. Genc[3], S. Ocak[1], A. Kendirci[2], D. Demirkol[4], Z. Bayramoglu[5], R. Tuna[1], M. Bilici[1], E. Akkaya[3], Z. Karakas[1]
[1]Istanbul University, Faculty of Medicine, Department of Pediatric Hematology-Oncology; [2]Istanbul University, Faculty of Medicine, Department of Orthopedia; [3]Istanbul University, Faculty of Medicine, Department of Biochemistry; [4]Istanbul University, Faculty of Medicine, Department of Pediatric Intensive Care; [5]Istanbul University, Faculty of Medicine, Department of Radiology

Baclground: FXIII deficiency cause a rare type of bleeding disorder and could be congenital or acquired. However, acquired form of FXIII deficiency may appeared from decreased production or increased consumption of FXIII by the antibodies against FXIII due to the autoimmune or neoplastic diseases Factor XIII also has some other roles in wound healing, bone extracellular matrix stabilization, and the interaction between embryo and decidua of uterus. Herein we report the development of inhibitor in a child with congenital factor XIII deficiency.

Case report: An-8-year-old boy with FXIII deficiency and bilateral developmental dysplasia of the hip has been admitted to orthopedics with severe pain and progressive decrease in the range of motions on bilateral hip joints. As he was on follow-up for cerebral palsy, epilepsy and hydrocephaly with VP-shunt, he was first referred to hematology clinic at the age of three for investigation of coagulopathy and diagnosed with FXIII deficiency (9%). During the follow-up, he was undergone operations like circumcision, orcihopexy and several small interventions for muscle spasticity. He was given FXIII concentrate once before each operation and just tranexamic acid and local fibrin-glue for small interventions with no significant bleeding. Due to severe pain and progressive immobility of the hip joints, a bilateral osteotomy was planned by orthopedics. The day before the operation, tranexamic acid was started and 500 U (20 U/kg) factor XIII concentrate were infused. On the day of the operation 500 U FXIII infusion was repeated. The surgery was performed without complication but after 24 hours of the operation, a rapid drop of hemoglobin count was noticed with bleeding in operation lodge and blood leak through the incisions. No major vascular leakage was seen on imaging. At the same time he was diagnosed with pneumonia and antibiotherapy was started. As the bleeding was persistent, he was given FXIII concentrate 1,250 U for one day and 500 U for 5 consecutive days. Factor level was found to be 10% after the infusion of the concentrate. The mixing test was positive for inhibitor with a titration of 8 BU. The bleeding was not controlled and after use of the all factor concentrates, he was given cryoprecipitate infusion daily and replacement with erythrocyte suspension on demand basis. The patient was started on corticosteroids and IVIG. Bleeding was continued on following two-weeks with increasing risk of compartment syndrome. Although inhibitor titer was decreased to 5 BU, in the light of the clinical bleeding anti-CD 20 monoclonal antibody was added to treatment for immunosuppression. After the fourth dose of the therapy, there was no bleeding anywhere, but inhibitör was still positive (1.4 BU). The infusion of high dose factor XIII concentrate (1,250 U) and sirolimus were given for the treatment of inhibitor positivity. Inhibitor was negative on day 10 of the treatment. Trimetoprim-sulfometaxasole was used for prevention of the infection Pneumocystis pneumonia and IVIG was given every 21 day. He had fever and vomiting. On the 7th day of the treatment, he had fever and vomiting. Leifsonia aquatica was detected in the blood and catheter culture. Meronem and vancomycine were started and cathater was removed. He was stabile and blood cultures were sterile after the therapy. But 19th day of the sirolimus therapy, respirator stress was develop and he was transferred pediatric intensive care unit. He died due to acute respiratory distress syndrome (ARDS), although all supportive therapy. Factor XIII activity was measured by photometric method by CS-2500 coagulation analyzer (Sysmex, Marburg, Germany). This method is based on ammonia release during transglutaminase reaction of FXIII. Released ammonia is measured via NADPH-dependent reaction photometrically.

Conclusion: Although FXIII deficiency is a rare bleeding disorder, precise and timely detection of the inhibitor against FXIII is important to initiate

appropriate treatment on time to remove inhibitors from the circulation in order to control bleeding and improve patient prognosis. In this respect, the coagulation laboratories have important responsibilities for examining factor activity and inhibitor levels using high accuracy and precision methods and contributing to patient treatment.

PP-120

Wait and watch, or test for anti-granulocyte antibody

Ç. Coşkun, F. Gümrük, Ş. Ünal
Hacettepe University Center for Fanconi Anemia and other inherited bone marrow failure syndromes

Background: Neutropenia in infancy and childhood poses a diagnostic challenge as the etiology ranges from acute life-threatening conditions to chronic benign diseases. Primary autoimmune neutropenia (PAN) in children is presented by severe neutropenia, but mild bacterial infections and spontaneous resolution. Anti-granulocyte antibody (AGA) testing is necessary or helpful in establishing the diagnosis. But detection of these antibodies frequently remains difficult. Here we report 2 cases with PAN who were diagnosed in AGA.

Case report: Case 1: A 10-month-old female patient presented with fever, nasal discharge. Complete blood count results are as follows, Hb 12.7 g/dl, white blood cells 4.9×10^3/μL, absolute neutrophil count (ANC) 0.8×10^3/μL, platelets (PLT) 248×10^3/μL. During the follow-up the patient was understood to have severe neutropenia when there was no infection, but has increase in ANC during infections. Serum IgG, IgM and IgA levels were normal. Additional samples were taken and sent to an off-site laboratory for congenital neutropenia mutations. Results were negative for all the known mutations. AGA were found to be positive. Patient is under follow up without treatment. Case 2: Neutropenia was detected at 9 months during a regular visit (ANC 0.9×10^3/μL). The baby had bronchiolitis for 3 times and otitis for two times and one hospitalization. The patient's growth and development were appropriate for his age. There was consanguinity between parents. During the follow-up, he had ANC levels mostly between $0.1–0.2\times10^3$/μL. For twice ANC $>1\times10^3$/μL was detected in the samples taken during the infection period. Bone marrow aspiration was performed at the age of one and was unrevealing. Cytogenetic analysis from the bone marrow was normal. Congenital neutropenia mutations were negative. The patient's AGA was found to be positive.

PAN has a benign, self-limited course and early diagnoses in AGA prevents unnecessary work-up and interventions. Both the cases tested positive for anti-neutrophil antibodies.

Conclusion: PAN is a rare disease in children. In most cases the diagnosis is suspected in a neutropenic patient after exclusion of other causes. In both our cases, absolute neutrophil count in the blood stream during acute infections were over 1×10^3/μL. Patients remained neutropenic outside these periods. AGA is helpful in diagnoses of PAN patients. PAN has a benign, self-limited course and early diagnoses in AGA prevents unnecessary work-up and interventions.

PP-121

Evaluation of the diagnostic power of the use of pediatric bleeding score in children with epistaxis

A. Alpcan, S. Tursun, M. Albayrak, M. Yorguc
Kırıkkale Unıversity Hospital

Background: Epistaxis is a common problem in pediatric population. Childhood epistaxis is rarely severe and seldom requires hospitalization. However, distinguishing normal from pathological bleeding is difficult in children. Hereditary mucocutaneous bleeding disorder can present with epistaxis too. Young children often may not show other bleeding symptoms, even if they have bleeding disorder. Evaluation of a child with bleeding symptoms begins with the investigation of child's age, gender, clinical presentation, history and family history. Therefore, to differentiate children with coagulopathy from normal and for standardization, Pediatric Bleeding Questionnaire (PBQ) have been improved. The Pediatric Bleeding Questionnaire (PBQ) was designed as a screening tool for von Willebrand disease (VWD) reported by Bowman. According to studies with bleeding symptoms, PBQ shows 83% sensitivity and 79% specificity for VWD. PBQ systematically scores each bleeding symptom according to the historically most severe bleeding episodes, using the sum of each individual symptom's score to evaluate the bleeding disorder probability.

Aim: In this study, we aimed to confirm PBQ as a VWD screening tool in children with epistaxis admitted to the hematology clinic.

Methodology: The study was approved by Kırıkkale University Faculty of Medicine (KUFM) Ethics Committee. Patients admitted to our outpatient clinic with epistaxis between January 2018 and January 2019 were evaluated retrospectively PBQ was performed by the same research assistant in the pediatric hematology outpatient clinic. Total bleeding score ≥2 was considered as a significant sign for VWD. Patients with a significant history of bleeding were evaluated with complete blood count, coagulation parameters, The Platelet Function Analyzer (PFA) -100, fibrinogen, factor levels and platelet function tests to investigate bleeding disorder.

Results: 120 patients were included in the study. Of these patients, 77 (64.2%) were male and 43 (35.8%) were female. Total of 22 (18,3%) patients showed clinically significant PBQ score of ≥2. VWD were detected in 9 of 22 patients (40.9%). In the remaining 98 patients whose PBQ was not significant, 4 patients were diagnosed with vWD. As a result, vWD was determined using PBQ in 9 (7.5%) of 120 patients. Using bleeding score has the following benefits; determining the severity of bleeding, providing compliance for health professionals in monitorization of bleeding, deciding treatment, preventing unnecessary laboratory tests, and minimizing false positive diagnosis. However, 4 patients (3.3%) could not be detected by PBQ. It should be kept in mind that the use of a bleeding score may cause problems in terms of taking time, not giving information about the severity and frequency of bleeding, and not ruling out bleeding diathesis.

Conclusion: According to these results, negative predictive value is high and positive predictive value is low. We wanted to make a difference in the development of bleeding scores and the use of non-invasive techniques such as bleeding score, because childhood operations, interventions and traumas were low.

PP-122

Health-related quality of life in children with acute lymphoblastic leukemia

E. Ocak, D. Kaçar, Ö. Üneri, H. Yaralı
SBÜ Ankara Hematoloji Ve Onkoloji Çocuk Sağliği ve Hastaliklari Suam

Objective: The importance of health-related quality of life (HRQOL) in patients with acute lymphoblastic leukemia (ALL) has increased in recent years. The aim of this study is to assess the HRQOL in children with leukemia and to evaluate the variables affecting the HRQOL. In this study, in addition to the evaluation of the quality of life of the patients, the thoughts of the parents on the quality of life of their sick children were also examined.

Methodology: A cross sectional study was performed including 2–12 years old children with ALL. Fifty-nine patients and their parents (mother and father) were enrolled and administered a Turkish version of the Pediatric Quality of Life InventoryTM (PedsQLTM) 3.0 Cancer Modules to determine HRQOL. Electronic data of patients were screened and the sociodemographical characteristics of the parents were questioned.

Results: Fifty-nine patients (52.5% male) with a mean age of 7.28±2.67 year and their parents were evaluated. According to subscales of self-report form; nausea and operational anxiety scores differ significantly by the treatment status; communication score differs significantly by the total length of stay; pain and hurt, cognitive problems and perceived physical appearance scores differ significantly by maternal chronic disease ($p<0.05$). The presence of maternal chronic disease was significantly related to the total score of PedsQL-cancer module parent-proxy report (mother) ($p<0.05$). We found moderate correlation between children and mother scores ($p<0.05$ $r=0.419$), however there was no correlation between children and father scores.

Conclusion: Children on-treatment had significant problems in nausea and procedural anxiety subscales, however children who hospitalized more, had fewer problems in communication subscale. Also, children whose mother

had chronic disease had poorer HRQOL regarding pain and hurt, cognitive problems and treatment anxiety. Given the importance of assessment and monitoring HRQOL in children with ALL, health professionals should be aware of how parental chronic disease effects HRQOL. Psychosocial support should be provided to children and their parents, especially whose parents have chronic disease.

PP-123

A rare case of gastric metastastasis from lung cancer

F. Teker
Gaziantep University

Background: Ekstratorasik metastases of non-small cell lung cancer (SCC) involves adrenal glands brain liver and lymph nodes. Metastasis to the gastrointestinal system particularly stomach is very rare. We herein describe an unusual case of gastric metastasis in a patient with squamous cell carcinoma of the lung.
Case report: Sixty-five-year-old men was operated by the reason of mass in the left lung. His TNM stage was T2N1 and received four courses of cisplatin and vinorelbine as adjuvant. After tere years in control tomography multiple suspicious lesions were seen in the liver. In PET scan it was seen multiple liver metastases, recurrent in the lung and multiple SUV accumulations in the stomach. Gastroscopy was performed and conducted biopsy. Pathological result was squamous cell carcinoma metastases of lung carcinoma. After he had received six courses of paclitaxel, carboplatin complete regression observed, he is on regular follow-up for six months and has no complaints.
Conclusion: Although there are some hypotheses the metastasis mechanism of gastric metastasis is not fully elucidated yet.

PP-124

Muscle strength is associated with activities and participation level in children with acute lymphoblastic leukemia undergoing consolidation therapy

V. Yıldız Kabak[1], F. Ipek[1], M. Dogan[1], S. Atasavun Uysal[1], S. Unal[2], T. Duger[1]
[1]*Hacettepe University, Faculty of Physical Therapy and Rehabilitation, Ankara, Turkey;* [2]*Hacettepe University, Faculty of Medicine, Ankara, Turkey*

Objective: Children with acute lymphoblastic leukemia (ALL) have problems in body functions, activities, and participation during treatments. We aimed to determine association between muscle strength and activity and participation level in children with ALL.
Methodology: This study was conducted at Hacettepe University, Ankara/Turkey. Children with ALL (n=18, 10 girl/8 boys) between the age of 5 and 10 (mean 6.88±1.37 years), receiving consolidation chemotherapy at outpatient clinic was included. Their mean duration after diagnosis was 22.5±7.85 months. Muscle strength was assessed with grip strength for upper extremity and 30 second sit to stand test (SST) for lower extremity. Pediatric Outcomes Data Collection Instrument (PODCI) was used to assess activities and participation level of the children.
Results: Mean grip strength was 6.64±3.86 and 6.11±4.29 kg/f for dominant and non-dominant hands, respectively. Mean SST score was 15.77±3.28 times. The SST was associated with subtest of PODCI-transfer and basic mobility (r=0.545, p=0.019). Dominant hand grip strength was associated with PODCI global functioning score (r=0.624, p=0.013).
Conclusion: Activity and participation level may give more information regarding "returning to normal life" for children with ALL. Muscle strength was found one of the predictors affecting activities and participation in this study. We suggest that interventions aiming to increase muscle strength will positively affect activities and participation level in children with ALL.

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