

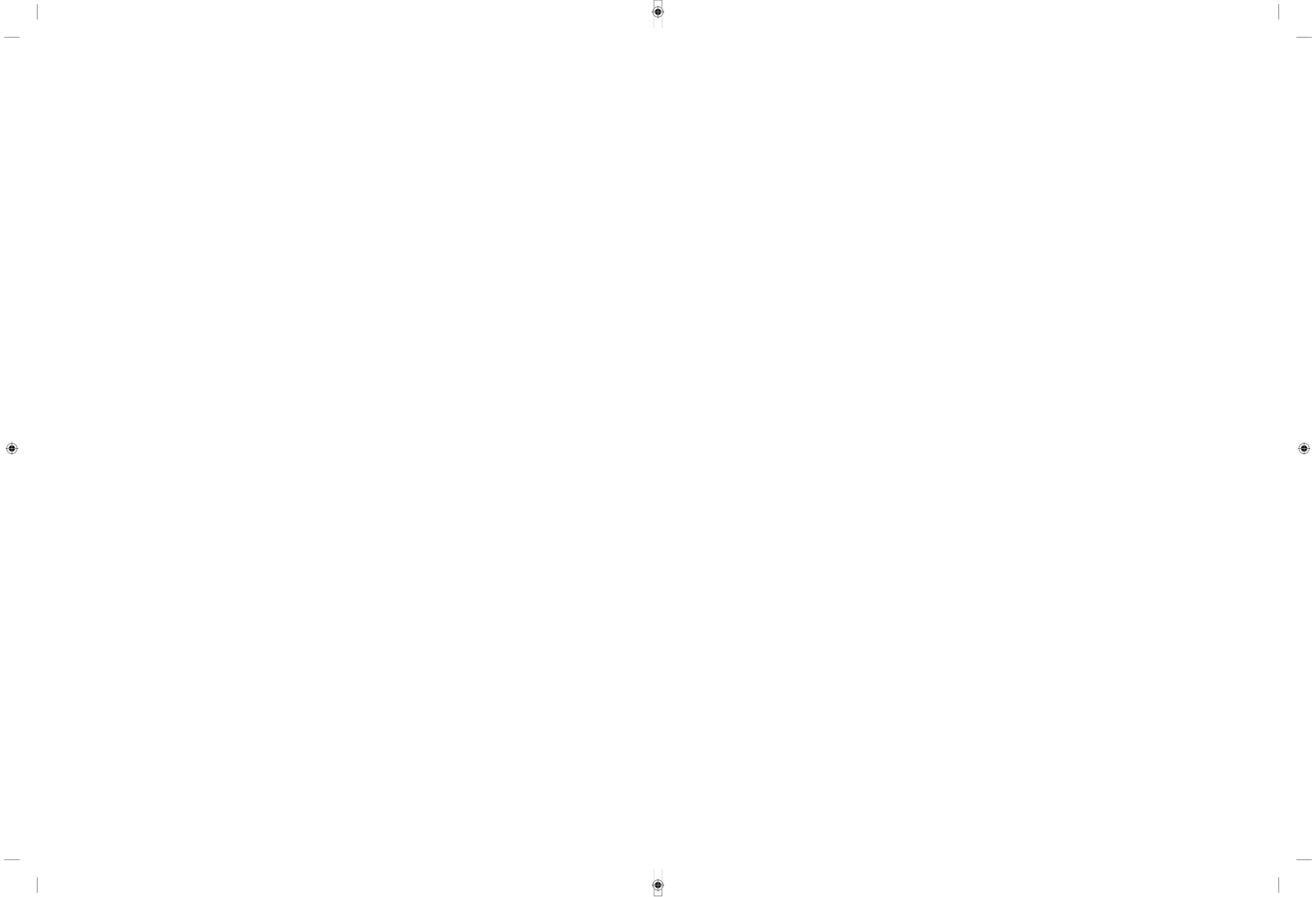
# HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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VOLUME 44, SUPPLEMENT 1, OCTOBER, 2022

# HEMATOLOGY, TRANSFUSION AND CELL THERAPY

VOLUME 44,  
Supplement 1,  
October, 2022



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## **XIII Eurasian Hematology Oncology Congress**



### **Abstract Book**

**5-8 October 2022**



Symposium abstracts are published as submitted or with minor editing only.  
*Hematology, Transfusion and Cell Therapy* is not responsible for errors or omissions  
in the abstracts.

## Welcome Address

Dear Colleagues,

We are happy to meet you at XIIIth Eurasian Hematology-Oncology Congress will be held as a face-to-face congress between 5-8 October 2022 at Hilton İstanbul Bomonti Hotel & Conference Center.

We believe deep in our hearts that with its special online concept, EHOc 2022 will fill in a significant gap in our region.

The attendees will be able to enjoy scientific programs in both Adult Hematology & Pediatric Hematology / Oncology as well as Nursing.

EHOc is collaborating with several international societies as usual including.

- **Brazilian Association of Hematology, Hemotherapy, and Cell Therapy (ABHH)**
- **European Society for Blood and Marrow Transplantation (EBMT)**
- **European Leukemia Network (ELN)**
- **Israel Society of Hematology and Transfusion Medicine**
- **Russian Oncohematology Society (ROHS)**
- **Society of Hematologic Oncology (SOHO)**
- **Society of Hematologic Oncology Italy (SOHO Italy)**
- **Society of Medical Oncology Pakistan (SMOP)**

Additionally Pediatric Hematology and Pediatric Oncology programs will be co-organized with the Turkish Pediatric Hematology Association and Turkish Pediatric Oncology Group Association.

There will be online oral and poster presentation sessions.

We hope that you will benefit in the best way possible of EHOc 2022.



Birol Güvenç  
President of Hematology Specialist Association



Giuseppe Saglio  
President of EHOc 2022  
President of EHOc

## Hematology Specialist Association

President



Birol Güvenç

Vice President



Serdar Bedii Omay

Secretary General



Şehmus Ertop

## Board Members



Ali Ünal



Sevgi Kalayoğlu Beşişik



Oktay Bilgir



Orhan Ayyıldız

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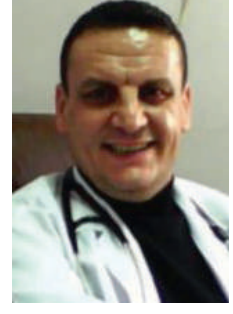
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President of EHOOG  
Giuseppe Saglio



President of Hematology  
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Birol Güvenç



Vice President of  
Hematology Specialist  
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Serdar Bedii Omay



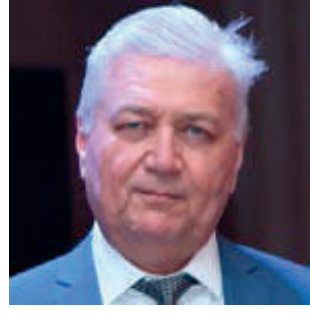
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Pediatric Program Coordinator  
Bülent Antmen



President of Turkish Pediatric  
Hematology Association  
Özcan Bör



President of Turkish Pediatric  
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Nurdan Taçyıldız

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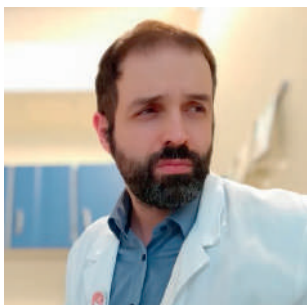


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Zeynep Karakaş  
Zühre Kaya

## Chairs and Speakers Biographies



### **Alessandro Lucchesi**

Scientific Institute of Romagna for the Study and Treatment of Tumors (IRST) IRCCS, Meldola, Italy

Senior Consultant (Hematology), Researcher (IRCCS network, Italian Ministry of Health), Project Leader of the "MPN and rare hematological diseases" institutional program.

Alessandro Lucchesi, MD, PhD, is a clinical hematologist and a researcher in the field of myeloproliferative neoplasms (MPNs). He started studying blood diseases in 2003 at the “Seràgnoli” Institute of Bologna, where he structured one of the larger data collections on the standard treatments of Essential Thrombocythemia. After his graduation he moved to L’Aquila where he completed the residency/fellowship program under the guidance of Prof. Guglielmo Mariani and Prof. Antonio Tabilio. During this experience, in addition to consolidating his interest in MPNs, he trained in Internal Medicine and worked on coagulation disorders. After a violent earthquake struck the city of L’Aquila in 2009, Dr. Lucchesi dedicated himself to the reorganization of primary care services. In 2011, he joined the IRST IRCCS of Meldola, where he started contributing to clinical and preclinical research. Since 2012 he has been studying some peculiarities of the hemostatic processes in MPNs. Dr. Lucchesi is currently a highly specialized physician, a senior researcher, and a member of the Phase 1 Clinical Trials Unit.



**Ali Taher**

American University of Beirut Medical Center, Beirut, Lebanon

Professor of Medicine at the Division of Hematology & Oncology Department of Internal Medicine, Director of the Naef K. Basile Cancer Institute (NKBCI) and Associate VP for Medical Advancement and Communications at the American University of Beirut Medical Center

He currently occupies the position of the Vice Chair for Research at the Department of Internal Medicine, AUBMC

In May 2018 Prof. Taher was granted Tenure in the current rank as full time professor in the Department of Internal Medicine, Faculty of Medicine at AUBMC.

In November 2020, an international study produced a composite citation based indicator and listed Prof. Taher among the world's top 2 percent of scholars in his respective field.

Prof. Taher has been invited to over 200 conferences both regionally and internationally as a keynote speaker, chairperson and moderator and has around 450 manuscripts published in leading peer-reviewed international journals

He is also an active member of some of the most prestigious Hematology societies in the world including the American Society of Hematology (ASH), European Hematology Association (EHA), and The International Society on Thrombosis and Hemostasis (ISTH)

In November 2021, Prof. Taher was recognized and placed in the top 0.1% of scholars writing about Anemia over the past 10 years by Expertscape's PubMed-based algorithms.

He is currently the chair of the EHA Scientific Working Group (SWG) on Red cells and Iron, member of the EHA Education committee and member of ASH Scientific Committee on Iron and Heme.

Most recently in June 2022, Prof. Taher was selected as the recipient of the 2022 European Hematology Association (EHA) Education and Mentoring Award.



### **Arnon Nagler**

Hematology, Tel Aviv University, Israel

- President Hemato-Oncology Center, Chaim Sheba Medical Center, Israel
- Director of the Division of Hematology and BMT, Chaim Sheba Medical Center, Israel (2003-2020)
- Director of Cord Blood Bank, Chaim Sheba Medical Center, Israel
- Professor of Medicine at the Tel Aviv University, Tel Aviv, Israel
- Chair of the ALWP of the EBMT: 2014-2018
- Vice chair of the ALWP of the EBMT: 2018-
- coChair Scientific Council of the EBMT : 2016-2018
- One of the pioneers of the non-myeloablative and reduced intensity/toxicity allogeneic transplantations for both malignant and non-malignant disorders (Blood 1998)
- Established the first public cord blood bank and performed the first cord blood transplantation in Israel
- Active member of the EBMT since 1993
- Leader of the Alternative donor subcommittee of the ALWP of the EBMT from 2008-2010
- Leader of the RIC subcommittee of the ALWP of the EBMT –2010-2014
- Member of multiple national and international societies and committees
- Serves on the Editorial Board of several BMT and Hematology Journals and is a Section Editor for *Leukemia*

Arnon Nagler, M.D., M.Sc., is director of both the Division of Hematology and the Bone Marrow Transplantation and Cord Blood Bank at the Chaim Sheba Medical Center, Tel-Hashomer, Israel and Professor of Medicine at The Tel Aviv University, Tel-Aviv, Israel.

Dr Nagler received his medical training at the Hebrew University-Hadassah Medical School, Jerusalem, Israel, specializing in Internal Medicine and Haematology at the Rambam Medical Center, Haifa, and in Hematopoiesis (MSc) in TA University, Israel. He carried out a Postdoctoral research fellowship in hematology and bone marrow transplantation at "Stanford University Hospital" Palo Alto, CA, in the USA, from 1986 to 1990.

Dr. Nagler has been working in the fields of bone marrow transplantation for haematological malignancies, for the last 25 years. Dr Nagler is one of the pioneers of the non myeloablative and reduced intensity/toxicity allogeneic transplantations for both malignant and non-malignant disorders (Blood 1998). His main contributions and scientific interests include hematopoietic stem cell transplantation, haematological malignancies, cord blood biology and transplantation and adoptive cell-mediated immunotherapy including NK cell biology.

Dr Nagler established the first public cord blood bank in Israel and performed the first cord blood transplantations from related and unrelated donors in genetic and malignant hematological diseases in Israel.

Dr Nagler is active member of the EBMT since 1993. In 2001 EBMT Annual meeting (Maastricht, the Netherland) his study on IL-18 for GVHD in mice model was chosen for presentation at the presidential symposium. Over the years he was invited speaker in several of the EBMT meetings. Dr Nagler served as the leader of the Alternative donor subcommittee of the ALWP of the EBMT from 2008-2010 and from 2010 -2014 was the leader of the RIC subcommittee of the ALWP of the EBMT.

Dr Nagler serves on the Board of Directors of Netcord organization of cord blood banks and was the Netcord Treasurer from 2010-2013.

Dr Nagler is a member of multiple national and international societies and committees in the field. He serves on the Editorial Board of several journals and was the stem cell transplantation Section Editor for *Leukemia* and is currently Associate editor of *BMT* and served Editorial Boards of numerous Journals in the field of stem cell transplantation and hematology .

Dr Nagler has written numerous original articles, reviews and chapters for top rank peer-review journals including JCO, Blood, JEM, JI, EJI ,Leukemia and many others and is the principal investigator for a multiple clinical studies including first to human trials with novel molecules like Pidilizumab (McAb against PD-1) and BL8040 (novel CXCR4 antagonist). Dr Nagler is inventor of multiple patents including for purging of BM with NK cells and inhibition of fibrosis by Halofuginon.

Dr Nagler has received several awards including the best scientific abstract award of the ASBMT/CIBMR Tandem meeting (2004) and the best clinical abstract award of the NMDP Council Meeting (2004). In addition, Dr Nagler is a popular speaker and has made numerous, invited, international presentations and many Oral presentations on almost annual basis in all international transplantation and haematology meetings - ASH,ASBMT/CIBMTR, EBMT, EHA, Exp Hematology (including a presentation at the presidential symposium) and invited presentation at the Gordon conference (Boston USA).



**Dildar Bahar Genç**

University of Health Sciences, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey

Graduated from Istanbul University, Cerrahpasa Medical Faculty (English Department) in 1995, and completed her pediatric residency program at Istanbul University, Cerrahpasa Medical Faculty in 2001. After two years of practice as a pediatrician, she completed her pediatric oncology residency program at Marmara University Medical Faculty in 2008. She became an associate professor of pediatric oncology in 2016. Currently, Dr. Genç works at the University of Health Sciences, Sisli Hamidiye Etfal Training and Research Hospital, Department of Pediatric Oncology. She is the Vice-Chair of the Subcommittee on Measurement and Assessment in Pediatrics at Health Sciences University and the Chair of the Subcommittee on Measurement and Assessment of Turkish Board of Pediatrics. Dr. Genç is a member of SIOP (Société Internationale D'oncologie Pédiatrique), and Turkish Pediatric Association, and board member of TPOG(Turkish Pediatric Oncology Group).



### **Carmino Antonio De Souza**

Hematology, Health Secretary of Campinas City - São Paulo State and Director of Hematology and Hemotherapy Brazilian Association (ABHH), Brazil

Professor Carmino Antonio De Souza, e-mail "carmino@unicamp.br", 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 1997-1998. Onco hematologist, working in the Malignant Lymphomas, Chronic Myeloid Leukemia and Bone Marrow Transplantation.

He has about 390 published scientific 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 - 48 and Hi10 index - 153 and about 10700 citations (Google Scholar – 25th July 2022). Author of one non scientific own book and 150 newspaper articles, all in Portuguese.

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 Italian Association of Hematology). Head of the Hematology and Hemotherapy Center 1985 – 1993 and 2006 – 2011. São Paulo State Minister of Health – 1993 – 1994. Campinas City Secretary of Health between 2013-2020, Scientific Director of Brazilian Hematology and Hemotherapy Society (SBHH) – 2005-2009 and President of Brazilian Hematology, Hemotherapy and Cell Therapy Association (ABHH) – 2010-2013.

### **EDUCATION/TRAINING**

Year Title or activity Institution

1970 - 1975 Graduation in Medicine University of Campinas, São Paulo, Brazil

1976 - 1978 Medical Residency University of Campinas – São Paulo –Internal Medicine and Hematology Department

1987 Doctoral Thesis School of Medicine, Campinas-SP, UNICAMP

Post Doctor Training

1997 - 1998 University of Genoa – Italy – Ospedale San Martino – tutor - Dr. Gino Santini – Aggressive Malignant Lymphomas



**Dieter Hoelzer**

Hematology, Onkologikum Frankfurt, Germany

Dieter Hoelzer is a former Professor of Medicine and Hematology and an expert on acute leukemias.

He founded the German Adult ALL Study Group (GMALL) with 7 multicenter studies in >145 participating hospitals and the European Working Group on Adult Acute Lymphoblastic Leukemia (EWALL).

He currently chairs the Medical Advisory Board of the German Carreras Leukemia Foundation, Advisory Board member of the Society for Hemato-Oncology (SOHO) and 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 an honorary member of the Hematological Societies of Austria, Hungary and Germany (DGHO) and received the doctor honoris causa from the University of Athens and Pavlov First St. Petersburg State Medical University.

Prof. Hoelzer is author or co-author of more than 800 peer-reviewed publications and co-author of international textbooks, such as Oxford textbook of Oncology, the forthcoming 21st Edition of Harrison’s principles of Internal Medicine and an editorial for the New England Journal of Medicine





### **Evangelos Terpos**

Stem Cell Transplantation Unit 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 bone disease in multiple myeloma and has evaluated the effect of bone-targeted agents and of different anti-myeloma therapies on bone metabolism of myeloma patients. Dr Terpos has studied the role of modern imaging (including WBLDCT and DWI-MRI) for myeloma, and he is also interested in the role of MRD in plasma cell neoplasms. During COVID-19 pandemic, Dr Terpos evaluates the kinetics of humoral immunity after COVID-19 and after immunization against SARS-CoV-2 in cancer patients and especially in patients with plasma cell neoplasms.

In the clinical research era, Dr Terpos is the PI in several investigator-initiated phase 1/2 studies for myeloma and has participated in the majority of phase 3 studies with novel agents in the myeloma field. His research work was reported in more than 650 papers in peer-reviewed journals and Dr Terpos has more than 30,000 citations and an h-index of 81 in ISI/Web of Knowledge and more than 44,000 citations and an h-index of 100 in Google Scholar (July 2022).

Dr Terpos is co-chairing the Bone Sub-Committee of the International Myeloma Working Group and is a member of the Guideline Subgroup of the European Myeloma Network. He is also a member of the Education and Publication Committees of the International Myeloma Society (IMS) and Editor in Chief of the IMS Newsletter.

He has given lectures at ASH, ASCO, EHA, EMN meetings and International Myeloma Workshops. He is Associate Editor of *HemaSphere* for Myeloma (official journal of EHA) and member of the Editorial Board of *Blood Cancer Journal*, *American Journal of Hematology* and *Haematologica*.



**Galia Stemer**

Galilee Medical Center, Nahariye ,Israil

Dr. Stemer received her medical degree from the Faculty of Medicine at Hebrew University and specialized in Internal Medicine at Beilinson and Meir MC's followed by a specialty in Hematology at Rambam MC. Between 2009 and 2021, Dr. Stemer was a senior hematologist in Ha-Emek MC, specializing in the field of myelodysplastic syndromes and leukemia. During her work there she implanted novel and advanced treatment protocols and gained a lot of experience treating frail AML patients as well as MDS patients. Dr. Stemer has a special interest in genetics of myeloid malignancies and serves as principal investigator in many clinical trials. Dr. Stemer is the secretary of the Israeli MDS and Bone Marrow failure working group, a member of the Israeli Leukemia working group and Israeli MPN working group. She is also a member of the Israeli Hematology and Transfusion Medicine board. Since November 2021, Dr. Stemer serves as Head of Hematology Institute in Galilee Medical Center, Nahariya where she is leading and developing the field of myeloid malignancies, with an emphasis on diagnosis and treatment of MDS patients.



**Hale Ören**

Pediatric Hematology, Dokuz Eylül University, Turkey

Hale Ören, MD, is a professor of pediatrics and a pediatric hematologist in the Dokuz Eylül University Faculty of Medicine, İzmir, Turkey. She is the head of the Department of Pediatric Hematology.

The main areas of Dr Ören's research are childhood leukemias, hemostasis, and thrombosis. She chaired the Turkish Pediatric Hematology Association and co-chaired the Turkish Society of Hematology, and still works in national leukemia and hemostasis/thrombosis subgroups.

Dr Ören has authored or co-authored more than 100 peer-reviewed papers in varied SCI/SCI-extended journals. She has written articles and has given lectures on the diagnosis, clinical and laboratory findings, follow-up, and management of leukemia, thrombosis, and bleeding disorders. She is a member of the editorial board for the Turkish Journal of Hematology.



**Hanan Hamed**

Ain Shams University, Cairo, Egypt

Professor of Internal Medicine and Clinical Hematology Faculty of Medicine Ain Shams University from October 2004 - till now.

Member of Hematology Board at Faculty of Medicine Ain Shams University.

Member of Bone Marrow Transplantation Board at Faculty of Medicine Ain Shams University. Head of Internal Medicine and Clinical Hematology Unit Ain Shams University Specialized Hospital ASUSH Cairo – Egypt. Till February 2019.

Member of scientific committee of Internal Medicine and clinical Hematology in Supreme Council of Universities in Egypt.

Vice president of Egyptian society of Hematology.

**Qualifications:**

MB Bch, December 1983 Faculty of Medicine Ain Shams University

M Sc Internal Medicine, April 1988 Faculty of Medicine Ain Shams University

M D Internal Medicine, April 1994 Faculty of Medicine Ain Shams University

Full training program in “Medical Response to Nuclear Accidents” in collaboration with Radiation Emergency Assistance Centre/ Training Site REACTS - Oak Ridge Institute of Science 1994

**Member of:**

American Society of hematology ASH

European Hematological Association EHA

International Society of Hematology ISH

Society of Hematologic Oncology SOHO

International Union of Angiology IUA

Egypt representative and ambassador Eurasian hematooncology group EHOg.

Pan-Arab hematology association

Founder and Adult hemato-oncology director in Middle East and North Africa Hematology League MENAHL.

Egyptian Hemato-oncology group EHOg

Egyptian Society of Hematology ESH

Egyptian Group of Hemostasis and Thrombosis

Egyptian Society of Oncology

Egyptian Society of Vascular Diseases and Surgery



**Jean-Francois Rossi**

Hematology, Montpellier University, France

Jean-Francois Rossi is professor of Hematology at the University of Montpellier. He studied at the Faculty of Medicine of Montpellier with a post-doctorate at Tuscon Az University and he was a research fellow at the NIH and in San Antonio Tx. He is board certified in rheumatology, immunology, internal medicine, medical oncology and hematology. He was head of the hematology department at Montpellier University Hospital for 18 years and develops research in Immune and Cellular Therapy, with Inserm and at the Avignon-Provence Cancer Institute. He is a consultant for various pharmaceutical companies and has participated to the creation of 3 start-up companies in biology and cellular therapy. He has 207 publications and received an AACR award in 2017 for his work on inflammation and interleukin 6, more recently developing the optimization of anti-IL6 therapies through mathematical model. He is member of different international scientific societies.

**Murat Özbalak**

Ağrı Research and Training Hospital, Division fo Hematology, Turkey

Murat Özbalak was graduated from Istanbul University Cerrahpaşa Medical School English Program in 2009. He completed the internal medicine residence in the same faculty in 2015. After 3 years of work experience, he started hematology fellowship in Istanbul University Istanbul Medical Faculty in 2015 and completed the program in 2021. Meanwhile, he continues a PhD program in the Immunology department of Istanbul University Aziz Sancar Experimental Medicine Institute. His research interests are focused on real-world results of lymphoma patients and lymphoma microenvironment.

**Piera Sivera**

Mauriziano Umberto Hospital, Turin, Italy

Piera Sivera was born on 11 November 1964 in Turin, Italy

**EDUCATION and TRAINING**

She graduated in Medicine and Surgery at the University of Turin in 1991, with the thesis: “Bone marrow transplant in haematological malignancies – Turin-based case series”

She achieved Internal Medicine residency in 1998, with the thesis: “Analysis of genetic mutations associated with hereditary thrombophilia – Literature review and personal case studies”

**CLINICAL and PROFESSIONAL EXPERIENCE**

From 1999 to 2004 she worked as an Internist at the Emergency Department of Mauriziano Umberto I hospital of Turin

Since 2005 she works as at the Haematology and Cell therapies Department of Mauriziano Umberto I hospital of Turin, where she is responsible for the haemorrhagic and thrombotic coagulopathy consulting room

Since 2017 she is coordinator of GET (Haemostasis and thrombosis group) Piemonte and Valle d’Aosta - She is regional representative for the Mauriziano hospital of Turin for thrombotic and haemorrhagic diseases

She participated as a speaker in several conferences of Haemostasis and thrombosis about chronic idiopathic autoimmune thrombocytopenia and venous and arterial thrombotic diseases

She organizes conferences about venous and arterial thrombotic diseases

She works as a tutor of internal medicine residents.



**Salam Alkindi**

Sultan Qaboos University, Muscat, Oman

Following my graduation from Trinity college- Dublin Ireland, in 1993, I have completed my general medicine as well as haematology/ oncology training in Dublin, Ireland and Fred Hutch cancer centre in Seattle USA, where I did my training in Bone marrow transplant. In 1999 I have joined Sultan Qaboos University and in 2005 I was appointed as head of department of haematology for 10 years. Previously also I held the position of deputy director of Sultan Qaboos university hospital for clinical affairs (clinical director) for 5 years. Research interests include sickle cell disease, chronic leukaemia and autoimmune disorders with over 100 articles published in international peer reviewed journals including NEJM, haematologica, and blood.

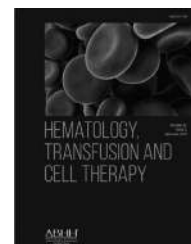


**Tiziano Barbui**

Ospedale Papa Giovanni XXIII, Bergamo, Italy

Tiziano Barbui was graduated at the University of Padua (Italy) where he where he received the rank of professor of Hematology. He was Consultant in Hematology at San Bortolo Hospital in Vicenza and founded the Department of Hematology at the Ospedali Riuniti di Bergamo. He headed the the Department of hematology and Oncology until 2008. Since 2008, professor Barbui is the Scientific Director of the Research Foundation at Hospital Papa Giovanni XXIII, Bergamo (Italy). He has served as Chairman on the Subcommittee on Lupus Anticoagulant of the International Society of Thrombosis and Haemostasis, and as President of the Italian Society of Hematology. Currently, he leads the EuropeanLeukemia-Net WP-9 on Myeloproliferative Disorders andwas the former Director of the Italian GIMEMA group on Philadelphia negative myeloid neoplasms. He is one of the founders of the NIH (US) Myeloproliferative Disorders Consortium. Currently, he was appointed by the European Hematology Association (EHA) as member of the governance board of the society. Professor Tiziano Barbui published so far more than 700 scientific articles in International peer reviewed journals (h-index 120) and is the Author of many books on Myeloproliferative Neoplasms. He significantly contributed to many fields of general hematology. The most cited articles refer to the Lupus anticoagulant syndrome, the hemostatic disturbances and therapy of acute leukemia, the optimization of diagnosis, prognosis and treatment of myeloproliferative neoplasms (MPN). In his position as head of the European Leukemia Net (ELN), he organized numerous guidelines for the management of ET, PV and PMF and for the definition of response criteria to be used in clinical trials of MPNs. He has been the principal investigator in several academic clinical trials published in the New England Journal of Medicine on Myeloproliferative Neoplasms and in the last session of WHO dedicated to the new classification of MPN (2017), he was asked to review the current concepts for the diagnostic criteria of Polycythemia Vera. Prof. Barbui received the gold medal from the Bergamo City Hall for his for his dedication to caring for patients with severe hematologic diseases and for his contribution to the advance of the hematological science. During the European Hematology Association (EHA) meeting in Stockholm (2013), he received the Jean Bernard award for his contribution to optimization of diagnosis, prognosis and therapy of the Myeloproliferative neoplasms and for establishing international networks for clinical research in Hematology. Prof Barbui, currently directs numerous observational studies on SARS-CoV12 infection in MPN patients and is the principal investigator of European studies on the optimization of MPN management.





## SPEAKER PRESENTATIONS

### ADULT SPEAKER PRESENTATION

Sp01

#### WILL IMMUNE THERAPY CURE ACUTE MYELOID LEUKEMIA?

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There is considerable recent progress in using immune therapy to treat lymphoid including monoclonal antibodies, antibody-drug and -radionuclide conjugates, bi-specific antibodies and chimeric antigen receptor T-cells (CAR-T-cells). Targets of these therapies are B-cell lineage-specific antigens such as CD19, CD20 and BCMA, not cancer-specific antigens. Given these immune therapy advances in lymphoid cancers one might expect similar success using immune therapy to treat acute myeloid leukemia (AML). However, this is not so. There is only one FDA-approved therapy of myeloid cancers, gemtuzumab ozogamicin (Myelotarg<sup>®</sup>) for AML approved > 10 years ago. Why this discordance? The answer lies in two considerations: (1) lack of a robust AML-specific target antigen(s); and (2) unacceptable adverse effects resulting from non-specificity of lineage-specific antigens such as CD33 and CD124. Also, most data suggest less immune surveillance against myeloid cancers compared with lymphoid cancers. For example, AML cells have an average of 0.28 mutation per megabase of DNA compared with 8.15 mutations for lung cancer, 40-fold less. The exception is the anti-AML effect associated with haematopoietic cell transplants, so-called graft-versus-leukaemia (GvL). However, this effect occurs only in an allogeneic setting and is difficult or impossible to distinguish from graft-versus-host disease (GvHD). We can envision potential anti-AML immune therapy using two strategies: (1) antibodies; and (2) cell therapies. Synthetic biology may offer a solution to the problem of the lack of an AML-specific target antigens. I discuss the current state of immune therapy of

AML and potential future directions. So, will immune therapy cure AML? Stand by.

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Sp02

#### BRENTUXIMAB VEDOTIN VERSUS CHECKPOINT INHIBITORS: WHICH ONE? WHEN? WHY SHOULD BE PREFERRED?

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About 15% of classical Hodgkin lymphoma (cHL) patients remain refractory to first-line therapy and about one third of the responding patients relapse<sup>1</sup>. The standard of care for relapsed or refractory (R/R) cHL is salvage chemotherapy followed by high-dose chemotherapy (HDCT) and autologous stem cell transplantation (ASCT)<sup>2</sup>. Three novel agents effective in R/R cHL were introduced; brentuximab-vedotin (BV), anti-CD30 antibody-drug conjugate<sup>3</sup> and the programmed-death-1 (PD-1) blocking antibodies, nivolumab and pembrolizumab<sup>4, 5</sup> has been approved. The optimal line to incorporate these agents is an actual dilemma. BV and PD1-blockers are effective in R/R cHL after ASCT. KEYNOTE-204 study reported that pembrolizumab treatment was associated with significantly longer PFS compared with BV (median:13.2 vs 8.3 months)<sup>6</sup>. In case of durable responses with PD1-blockers, cessation of the treatment may be an individualized decision and high response rates to re-treatment with PD1-blockers is an important advantage<sup>7</sup>. There is not obvious differences in the efficacy and toxicity of nivolumab and pembrolizumab<sup>8</sup>. We can conclude that PD1-blockers could be preferred over BV in patients who relapse following ASCT and who are naïve to BV and PD-1 blockade. For patients relapsing after ASCT with prior BV or PD1-blocker exposure, selection of the agent

that has not been used previously could be recommended<sup>8</sup>. BV and PD1-blockers are incorporated into the pre-ASCT salvage regimens in clinical trials. In the phase II BRaVE study, BV added to DHAP provided a complete metabolic response rate of 81% before ASCT, with a 2-year PFS and OS rates of 74% and 95%, respectively<sup>9</sup>. Similarly, pembrolizumab in combination with GVD provided an overall response rate (ORR) of 100%<sup>10</sup>. BV and nivolumab combination resulted in an ORR of 85%. The 3-year PFS rate for ASCT group was 91%<sup>11</sup>. Regarding these data, the need for ASCT will be an important point of debate in the next years. In case of primary refractory disease, chemotherapy-based salvage regimens remain the standard. Combination treatment with BV and nivolumab resulted in a 21-month PFS of 65% in this group<sup>11</sup>, which may be a satisfactory option in the future. Post-ASCT consolidation with BV is now standard of care in patients with risk factors defined by AETHERA trial<sup>12</sup>, which is supported by real-world data including pre-treated with and responsive to BV patients<sup>13</sup>. Novel agents are not recommended in the front-line management of early-stage disease. ECHELON-1 study performed on treatment-naïve stage III/IV cHL patients reported 6-year PFS, and OS ratio were 82.3% and 93.9% for BV-AVD cohort versus 74.5% and 89.4% for ABVD cohort<sup>14</sup>. Beside advanced stage cases, BV-based therapies should be considered for elderly, unfit patients who cannot tolerate combination chemotherapies, as they are associated with longer duration of response compared to BV monotherapy<sup>8</sup>. Giving decision about novel therapies, major adverse events, such as neuropathy for BV and immune related events for PD1-blockers. Optimal timing of BV and PD1-blockers and treatment strategies in case of resistance to novel agents are critical questions for the future of cHL management, which hopefully will be answered by the results of clinical trials and real-world data.

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### Sp03

#### TREATMENT OF MANTLE CELL LYMPHOMA IN TRANSPLANT NON-ELIGIBLE PATIENTS

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MCL is a rare but usually aggressive non-Hodgkin lymphoma that most commonly affects the elder population. It is now recognized as a heterogeneous disease with variable biologic and clinical behavior. MCL is considered incurable with current therapies and has historically been associated with a poor prognosis. Large gains were made in the first decade of the new century when clinical trials established the importance of high-dose therapy and autologous stem-cell rescue and high-dose cytarabine in younger patients and the benefits of maintenance rituximab and bendamustine in older patients. Patients with mantle cell lymphoma (MCL) usually respond to initial combination chemotherapy, but the disease inevitably relapses and often follows an aggressive course. Treatment paradigms have evolved along two lines. Younger,

fit mantle cell lymphoma (MCL) patients are generally treated with intensive strategies and older less fit patients with non-intensive strategies. Management of patients with newly diagnosed mantle cell lymphoma (MCL) depends on the age and fitness of the patient. For younger patients, the commonly accepted standard of care is a high-dose cytarabine-based induction chemotherapy followed by autologous stem cell transplantation (ASCT). In newly diagnosed patients with MCL ineligible for intensive therapy and ASCT, the standard-of-care has generally been R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), followed by rituximab, maintenance. In recent years, bendamustine-based therapy has been increasingly adopted for older MCL patients and more recently, vincristine has been replaced by bortezomib in the R-CHOP combination as VR-CAP for previously untreated patients. Traditionally, the treatment of MCL has been determined by patients being deemed “transplant-eligible” or “transplant-ineligible”. In particular, greater depth of understanding of the molecular pathophysiology of MCL has resulted in an explosion of specifically targeted new efficacious agents. In particular, agents recently approved by the Food and Drug Administration include the proteasome inhibitor bortezomib, immunomodulator lenalidomide, and Bruton's tyrosine kinase inhibitor ibrutinib. Newer data suggest more tolerable front-line therapy, including regimens incorporating novel agents, may produce similar outcomes to intensive historical induction regimens. This may in turn preclude fewer patients from autologous stem cell transplant and produce better long-term outcomes in transplant-ineligible patients. In the relapsed/refractory setting, novel agents and combination regimens are improving outcomes and changing the landscape of treatment. New therapies with distinct mechanisms of action, including novel immunotherapeutics, antibody-drug conjugates, and non-covalent BTK inhibitors, have demonstrated great potential for improving outcomes post-BTK inhibitor failure in relapsed/refractory mantle cell lymphoma. Although cBTK inhibitor has transformed the treatment landscape in B-cell malignancies, the majority of patients will eventually experience disease progression or treatment intolerance. There are 2 oral BTK inhibitors approved for use in relapsed MCL: ibrutinib and acalabrutinib. Acalabrutinib, originally referred to as ACP-196, is a novel, irreversible BTK inhibitor that was designed to be more kinase-selective than ibrutinib. Orelabrutinib is an orally administered, potent, irreversible and highly selective BTK-inhibitor being developed the treatment of B cell malignancies and autoimmune diseases. Tirabrutinib irreversibly and covalently binds to BTK in B cells and inhibits aberrant B cell receptor signalling in B cell-related cancers and autoimmune diseases. Zanubrutinib received accelerated approval in the USA on 14 November 2019 for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy, based on overall response rate (ORR) seen in phase II and I/II clinical trials. Palbociclib is a specific, potent, oral inhibitor of CDK4/6 capable of inducing a complete, prolonged G1 cell cycle arrest (pG1) in Rb+ MCL cells. Zilovertamab vedotin is an antibodydrug conjugate, which binds specifically to receptor tyrosine kinase-like orphan receptor-1 (ROR-1), an oncoprotein that is pathologically expressed in mantle cell lymphoma and other

malignancies. The development of anti-CD19 CAR T-cell therapy represents a major advance in the treatment of patients with chemorefractory B-cell malignancies.

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#### Sp04

##### HOW I TREAT DOUBLE-HIT LYMPHOMA AND HGBL, NOS

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**Introduction:** The new world health organization (WHO) classification on lymphoid neoplasms, the WHO-HAEM5, renames the former group that double-hit lymphomas were in as “diffuse large B-cell lymphoma/high-grade B-cell lymphoma with MYC and BCL2 rearrangements (DLBCL/HGBL-MYC/BCL2)”. This is mainly to highlight that the presence of MYC and BCL2 rearrangements form a unique phenotype, different than the MYC and BCL6 rearrangements (present in the former classification). Those lymphomas are composed of large or intermediate or blastoid cells, with aggressive clinical course and tendency to be resistant to standard chemotherapy. It's a group ideal for new therapies, such as the bispecifics and CAR T-cells, but lack data to support this since are underrepresented in clinical trials. Retrospective studies, with its inherent bias, consistently points to worst prognosis and poor outcomes with standard RCHOP treatment. How to best approach this hard-to-treat lymphoma is still a matter of debate. **Treatment considerations:** Roughly 65% of patients with DLBCL are cured with 6 cycles of RCHOP. When considering this regimen for HGBL, event-free survival (EFS) has been reported as low as 20% in 3 years. More intensive regimens, like R-DA-EPOCH and R-CODOX/M-IVAC, could increase this response, based on retrospective studies, with EFS 3y close to 80%. The role of autologous transplant as consolidation is controversial, and it's not routinely indicated. However, there are data that patients treated with RCHOP could increase progression-free survival (PFS) with this strategy, perhaps eliminating the difference between more intensive regimens. The lack of a direct comparison in a randomized phase 3 study between RCHOP or more intensive protocols precludes a firm conclusion. In the Alliance/CALGB 50303 study, that compared RCHOP with R-DAEPOCH in patients with DLBCL and PMBCL, there were no differences in 2y PFS between arms. But the number of patients with MYC rearrangement was too small to any conclusion regarding HGBL. Dunleavy et al conducted a phase 2 study with R-DA-EPOCH in 53 patients with MYC-rearranged DLBCL (24 were double-hit). EFS 4y was 71% and overall-survival (OS) 4y was 77%. Although this looks pretty good compared to the historic RCHOP, it's not a randomized study. New therapies have emerged as possible rescue in the relapsed/refractory DLBCL population, a group of

patients with a dismal prognosis. The chimeric antigen receptor (CAR) T-cells have become a new standard of care for those patients, when available. Albeit with a small number of patients, the three main products (axi-cell, tisa-cell and liso-cell), used for rescue of DLBCL patients, had shown activity against HGBL. That holds true in latter lines and as a first salvage treatment, as the recent trials comparing with autologous transplant. The zuma-12 is a phase 2 study with axi-cell as first-line of treatment with high-risk DLBCL patients, a population enriched with HGBL. Early reports are impressive, with nearly 80% of complete remissions. However, long term follow-up will be necessary to see with the responses are durable. Bispecifics are other very important players on that field, with the first reports of high activity in high-risk DLBCL, even after CAR T-cell failure. **Conclusions:** HGBL is an aggressive form of lymphoma, with tendency of a worst prognosis with conventional treatment. Intensive regimens seem to fare better than RCHOP, although with more toxicity and no randomized studies supporting this indication. New treatments, mainly CAR T-cells and bispecifics, are very promising and possibly will become standard of care for such patients but were in the therapy algorithm is still to be decided.

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#### Sp05

##### APPROPRIATE MANAGEMENT OF POLYCYTHEMIA VERA WITH CYTOREDUCTIVE DRUG THERAPY

##### EUROPEAN LEUKEMIANET 2021 RECOMMENDATIONS

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Classical Philadelphia-negative myeloproliferative neoplasms (Ph-neg MPNs) including polycythemia vera (PV), essential thrombocythemia (ET), and myelofibrosis (MF) are characterized by uncontrolled clonal proliferation of multipotent bone marrow progenitors, sustained by acquired mutations in JAK2, CALR and MPL genes. Expansion of the mutated clone triggers an inflammatory response that influences the development of associated vascular complications and disease progression into MF and acute leukemia. This presentation will focus on the recent recommendations by ELN in low-risk PV patients. According to ELN and NCCN patients with PV should be managed by the risk of thrombosis and cytoreductive drugs are recommended in high risk (over 60 y and/or prior thrombosis) while low-risk should be treated with low-dose aspirin and phlebotomy only. These guidelines have been reviewed by international recognized experts in the field of MPN. In January 2021, ELN promoted an international project specifically devoted to updating the clinical indications for using cytoreductive drugs in treating PV. The Expert Panel (EP), the chair and the methodologist were asked to grant the highest quality of the recommendations by adhering to standard methods for developing clinical practice guidelines, namely Grading of Recommendations Assessment,

Development and Evaluation (GRADE) (WHO Handbook for Guideline Development, 2011). These main questions will be presented and discussed. **Question 1** - What benefits should be expected from cytoreductive drugs over phlebotomy in “low-risk” PV patients? **Question 2** - Which “low-risk” PV patients might benefit from cytoreductive drugs? **Question 3** - Which cytoreductive drugs should be preferred in “low-risk” patients? **Question 4** - Which PV patients treated with HU should receive a different cytoreductive 223 drug? The results and recommendations were approved by Delphi consensus rounds and virtual meetings. The EP recommended that PV patients younger than 60 years old and/or free of prior thrombotic events start cytoreductive drug therapy if at least one of the criteria is fulfilled: 1) strictly-defined intolerance to phlebotomy, 2) symptomatic progressive splenomegaly, 3) persistent leukocytosis ( $> 20.000/mm^3$ ), 4) progressive leukocytosis 6) inadequate hematocrit control requiring phlebotomies, 7) persistently high cardiovascular risk, and 8) persistently high symptom burden. RoppegIFN or pegylated IFN- $\alpha$ -2a was the recommended cytoreductive drug for the above patients. Finally, the EP suggested that either rIFN $\alpha$  or ruxolitinib should be considered for patients treated with hydroxyurea but requiring a therapy change. The purpose of cytoreductive therapy is to obtain hematological responses, since normalizing blood counts with phlebotomy and/or cytoreductive drugs is thought fundamental to reduce the incidence of both arterial and venous thrombosis. However, despite achieving similar hematological responses, it is likely that the various cytoreductive drugs administered both in the first and second line do not have equal antithrombotic activity. In fact, for each of the three cytoreductive drugs currently used in clinical practice (Hydroxyurea [HU], Interferon [IFN], Ruxolitinib [Ruxo]), additional antithrombotic properties are recognized. For instance, HU is thought to have minimal anti-inflammatory properties [19], whereas there is evidence that IFN and Ruxo can normalize inflammatory markers, further mitigating thrombotic risk [20, 21]. Unfortunately, clinical trials comparing head-to-head the standard HU with IFN or Ruxo did not provide solid evidence of superiority of the latter in terms of thrombosis reduction. It should be noted, however, that the design of these studies envisaged hematological responses as primary end-points and the trials were not powered to directly evaluate a decrease in thrombosis risk. On the other hand, it is not yet demonstrated that hematological response is a valid surrogate of thrombosis [22-24]. Both the National Comprehensive Cancer Network (NCCN) and the European Leukemia Net (ELN) recommend a risk-stratified approach to the treatment of an individual patient and in ET and PV patients are [Treatment focuses primarily on mitigation of thrombosis risk and most patients with ET and PV should receive low-dose aspirin. As the prognosis for ET and PV varies substantially between patients, both the National Comprehensive Cancer Network (NCCN) and the European Leukemia Net (ELN) recommend a risk-stratified approach to the treatment of an individual patient [4,8]. This is exemplified by two large retrospective studies evaluating prognostic factors and outcomes among patients with MPNs [9,10]. Conventionally, patients age  $\geq 60$  years or with prior thrombosis are classified as high-risk [4]. However, the association of a higher thrombosis risk with the presence of JAK2/MPL

mutations in ET patients is increasingly recognized and included in the validated International Prognostic Score of Thrombosis in ET (IPSET) [5,11]. The impact of other factors such as leukocytosis in PV patients or the influence of comutations continues to evolve and is not part of the current guideline recommended approach to treatment selection [5,6,12–14]. Treatment focuses primarily on mitigation of thrombosis risk and most patients with ET and PV should receive low-dose aspirin [4,8,15]. prevention and treatment of major arterial and venous thrombosis in PV and ET with the aim to report: (i) quantitative estimates of major thrombosis incidence; (ii) rates of thrombosis under treatment with cytoreductive drugs; (iii) incidence of thrombosis under aspirin and oral anticoagulants.

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### Sp06

#### VACCINATION AGAINST SARS-COV-2 FOR MYELOMA PATIENTS: DO WE NEED A BOOSTER DOSE AND HOW FREQUENT?

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Patients with multiple myeloma (MM) are at increased risk for severe COVID-19 disease, hospitalization and death. In this context, it is essential to maintain an adequate immune profile. A third (first booster) dose has been offered with priority to patients with MM due to their immunocompromised status and the suboptimal immune response to the initial vaccination schedule against COVID-19. Three important studies that investigate the immune profile following a booster vaccination with a mRNA-based vaccine have been recently published. The first study was published in *Blood* (2022;139(9):1409-1412) by Terpos *et al* and included 167 consecutive patients with MM who were vaccinated with the booster BNT162b2. All patients had been fully vaccinated with the 2-dose BNT162b2. Median time between the second and the booster dose was less than 5 months. The booster dose significantly improved the median neutralizing antibody (NAb) response in patients with MM (27.1% before to 96.7% after the third dose  $p < 0.001$ ). Importantly, almost half of the patients with suboptimal NAb responses at one month after the second dose of BNT162b2 developed NAb titers of at least 50% at one month after the booster dose. Treatment with anti-BCMA agents emerged as a significant adverse predictive factor for NAb response to the booster shot. None of these patients achieved a NAb level above the positivity threshold. The second study was published in *Cancer Cell* (2022;40(5):441-443) by Aleman *et al* and included 261 patients with MM with available anti-SARS-CoV-2 spike (S) IgG measurements at least 1 week after the third vaccine shot. Anti-S IgG levels increased significantly after administration of the third dose both in patients with and without prior history of COVID-19 ( $p < 0.001$ ), although the depth of humoral response was inferior to healthy individuals. Importantly, 60 out of 68

seronegative patients before the third dose seroconverted with the booster shot. Neutralizing titers against the Omicron variant after the booster dose were detectable in only 54% of MM patients who responded to two doses of the vaccine (they had adequate protection against Wuhan variant) and in none of those who did not respond in the initial vaccine doses. The third vaccine shot significantly increased spike-specific CD4+ T cell-mediated cytokine responses, as well. The third study was published in *Cancer Cell* again (2022;40(6):587-589) by Enssle *et al* and included 71 patients with MM and 23 healthy controls. The authors observed a 4-fold increase in anti-S IgG levels from a median of 193.2 BAU/ml before to 776.0 BAU/ml after the booster dose in the MM cohort. However, a poor neutralization capacity against the Omicron variant was observed. Regarding cellular immunity, MM patients showed a significant T-cell response against the wild-type virus, the Delta variant and the Omicron variant, although the response was attenuated in the latter case. Overall, the abovementioned studies advocate for prioritizing patients with MM, especially those on anti-BCMA treatments, for additional booster shots, ideally with variant-adapted vaccines, or with the prophylactic administration of monoclonal antibodies against SARS-CoV-2. The standard vaccine seems not to prevent the infection with omicron variant(s) and thus general preventive measures including mask wearing and avoiding crowds remain important for these vulnerable patients.

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#### Sp07

##### REDUCED INTENSITY CONDITIONING FOR ALLOGENEIC STEM CELL TRANSPLANTATION (HSCT) IN ACUTE MYELOID LEUKEMIA

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Allogeneic transplantation (HSCT) is an effective curative therapy for high risk acute myeloid leukemia (AML) which account for 38% of the transplants in Europe (1). Prior to HSCT, a conditioning or preparative regimen is administered. The conditioning regimen has 2 components; one target the myeloid system aiming in eradication of the leukemic clones, while the other target the immune/lymphoid system to ensure engraftment and to prevent rejection. Some of the compounds used in the conditioning are more myeloablative in nature for example busulfan or melphalan) 2-4) while others are more lymphodepleting like fludarabine or Cytosan (5). Traditionally, the pre HSCT conditioning was myeloablative (MAC) and includes total body irradiation (TBI) in combination with cyclophosphamide (CY) (2-3). High-dose busulfan (Bu) is the most commonly used TBI-free-based myeloablative conditioning (2-3). In HSCT from unrelated or mismatched donors the pre transplantation conditioning typically includes serotherapy with anti-thymocyte globulin (ATG) or

the CAMPATH monoclonal antibody in order to avoid rejection and ensure engraftment while preventing graft versus host disease (GVHD) (5). However, the MAC is typically associated with significant morbidity and mortality due to the toxicity of the preparative regimen, GVHD, and the immune-deficient state that accompanies the procedure (2,5-6). This is especially true in patients above the age 55-60 years old and in patients with comorbidities which are the majority of AML patients. Extensive research, including pharmacokinetic and pharmacodynamics studies has been directed therefore towards the development of safer and less toxic conditioning regimens for HSCT, optimizing the conditioning allowing its applications to elderly patients and patients with comorbidities (2,5-6). These modern conditioning regimens which are based in part on the immune-mediated graft versus leukemia (GVL) effect are in principle low-dose, less toxic and tolerable conditioning regimens termed reduced intensity (RIC) with different immunosuppressive and myelosuppressive properties (5-7). These regimens combine immunosuppressive agents (such as fludarabine with or without serotherapy or targeted therapy with agents with moderate myelosuppressive effects or novel agents. However, they typically result in higher relapse rate especially in patients undergoing HSCT while not in remission and in patients with high risk leukemia including patients with adverse cytogenetics, high risk mutations and patients with positive measurable residual disease (MRD) at time of transplants. The optimal regimen is thus the one with intensive anti-leukemic activity, but with limited toxicity-the so called reduced toxicity regimens (RTC). These novel regimens are mostly fludarabine based and incorporate drugs like melphalan; thiotepa; treosulfan and clofarabine (8-11). Other protocols are the so called TBF protocol that include two alkylating agents like busulfan and thiotepa(9,11) and the FLAMSA protocol that includes fludarabine, cytarabine, and amsacrine (11).The RIC and RTC regimens enable HSCT in elderly patients and those with comorbidities reducing drastically transplant related mortality and organ toxicities in combination with improved anti leukemic effect. Efficient safe pre transplant conditioning protocols are continuing to be developed. Future protocols will most probably incorporate specific anti leukemic targeted novel compounds as well as monoclonal and radiolabeled antibodies.

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#### Sp08

##### LESSONS FROM THE EUROPEAN AND ISRAEL NATIONAL MDS REGISTRY

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On behalf of the Israeli MDS working group and EUMDS Registry/ XIII Eurasian Hematology Oncology Congress (EHOC) 2022. The myelodysplastic syndromes (MDS) are a group of clonal stem cell diseases with cytopenias and a tendency to transform to leukemia. Despite the progress, there is still lack of real world data about the disease. In 2008, top European experts

launched the EUMDS Registry. In this project, including 19 countries and 150 sites, epidemiological, clinical and lab data on newly diagnosed MDS patients, are collected and analyzed. As of today, 3300 patients have been recruited. In 2012, the Israel MDS group joined the project. We have contributed data on 360 patients, # 4 in the contributors. This project led to more than 100 abstracts in international meetings and 40 publications in first line journals. We will mention some of these studies. de Swart et al. summarized data on the first 1000 patients, validated the IPSS-R prognostic classification, showing its superiority on IPSS (de Swart L. *BJH* 2015). Another study, focusing on Quality of life (QoL) of LR-MDS patients revealed that these patients suffer from depression, anxiety, pain, discomfort and mobility difficulties, compared to controls (Stauder R, *Leukemia* 2018) The effects of Erythroid Stimulating Agents (ESAs,) was evaluated: Garelius et al. showed that ESA administration delays RBC transfusion dependency (Garelius HK. *J Intern Med* 2017). Since in most countries ESA is given to transfusion-dependent MDS patients, it might change the paradigm. Recently, we demonstrated that ESA treatment, is associated with improved outcomes and overall survival (Garelius HK. *EHA* 2022; submitted). Since prognostic factors are often determined at disease presentation, it was important to develop dynamic parameters. We showed that a rapid decline > 25% in the platelet count within 6 months is an adverse prognostic marker (Itzykson R. *Bl Adv* 2018) A study focusing on the mutational status was presented at ASH 2021 showing that LR-MDS patients can be grouped into 3 clusters, with a correlation to the clinical status (Malcovati L. *ASH* 2021) The Israeli group, independently and as a part of the EUMDS, was involved in several projects. Oster et al. suggested a non-invasive calculator to assess the probability of or excluding MDS diagnosis, based on patient characteristics, avoiding BM examination (Oster HS. *Bl Adv* 2021). We also investigated the correlation between Hb level and QoL. This correlation was found to be partial, and the decrease in QoL was not linear. This suggests that other factors other than Hb might play a role in determining QoL (Haring Y. *ASH* 2021). We recently presented data on lymphoid aggregates in BM biopsies, suggesting a possible association with poor prognosis (Book-Rabinowitz. *Int MDS Symposium*, Toronto 2021; submitted). **In summary**, the EUMDS registry is a platform of a scientific project, and an example of international collaboration. Such projects, especially in relatively uncommon diseases, allow collection of enough data to allow meaningful conclusions that might change paradigm and improve patient care. We call all participants of this meeting to join us and improve the quality of this wonderful important project.

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### Sp09

#### EMERGING DATA FOR CANCER ASSOCIATED THROMBOSIS TREATMENT

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Venous thromboembolism (VTE) is a common complication in patients with malignancies, resulting in deep vein

thrombosis, pulmonary embolism and central venous catheter VTE, and is responsible for high morbidity and mortality (1). The prevalence of cancer-associated thrombosis is increasing because of multiple factors, including longer patient survival, anticancer therapies, increased detection of incidental VTE during surveillance imaging, and wider use of central venous catheters. Anticoagulant therapy with low-molecular-weight heparins (LMWHs) was the standard of care for the treatment of cancer-associated thrombosis, with vitamin K antagonists providing a secondary treatment option, until direct oral anticoagulants (DOAC) emerged as alternative first-line treatment options in 2016 (2). Rivaroxaban, Edoxaban and Apixaban are recommended as initial treatment in patients with cancer-associated thrombosis who are not at high risk of gastrointestinal or genitourinary bleeding (3). LMWHs and Fondaparinux are still recommended for prophylaxis of VTE in medically-treated patients with cancer. Rivaroxaban and Apixaban can be used selectively for thromboprophylaxis in patients with malignancies at high risk of VTE, for example in patients with pancreatic cancer or myeloma (4,5). Anticoagulant choice should incorporate a personalised medicine approach that considers cancer type, VTE and bleeding risk factors, drug–drug interactions (DDI), and patient preferences. Patients with cancer often experience narrow therapeutic index polypharmacy and undergo treatment for several simultaneous comorbidities. In this setting the risk of DDI is high in particular during therapy with tyrosine kinase inhibitors (6). Concerns on DDI management include decreased efficacy and bleeding risk. In general, DOAC use is not advisable in combination with drugs that are strong inhibitors of both P-gp and/or CYP3A4 for high bleeding risk and in combination with strong inducers of Pgp and/or CYP3A4 that could markedly reduce DOAC plasma levels. Routine use of plasma level measurements for DOAC, only available in few laboratory centres, is not currently recommended (7). Nevertheless it has recently become increasingly clear that clinicians need to assess the anticoagulant status of a patient receiving anticancer therapies. The global coagulation Test of thrombin generation (TGT) a sensitive method to assess the anticoagulant therapy, provides a global measure of anticoagulant effect by measuring the inhibition of formation of thrombin (FIIa), a common endpoint for both LMWH and FXa inhibitors (8). Further studies are warranted to better define the future role of this coagulation test in this subgroup of patients.

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### Sp10

#### VASCULAR DISEASES IN PNH

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PNH is a condition in which uncontrolled complement activity leads to systemic complications, principally through intravascular hemolysis and platelet activation. It arises through a somatic mutation of the phosphatidylinositol glycan A (PIG-A)



gene in bone marrow stem cells, 1,2 resulting in disruption to glycosylphosphatidylinositol (GPI) biosynthesis, 3. Among the deficient proteins are the complement regulatory proteins CD55 and CD59, resulting in increased complement sensitivity of PNH cells, intravascular hemolysis, promotion of inflammatory mediators, and systemic hemoglobin release<sup>4</sup>. Patients with PNH can present with multisystemic clinical manifestations due to intravascular hemolysis, thrombosis and bone marrow failure<sup>5</sup>. Symptoms are therefore often non-specific, ranging from loss of vision (due to retinal thrombosis), headache and nausea/vomiting (due to cerebral thrombosis), pulmonary hypertension (due to pulmonary embolism), anaemia, through to pain and swelling in the lower extremities (due to deep vein thrombosis), renal failure and other symptoms affecting different systems<sup>6</sup>. Thromboembolism is the most common cause of mortality in patients with PNH and accounts for approximately 40% to 67% of deaths of which the cause is known. Further, 29% to 44% of patients with PNH have been reported to have at least 1 thromboembolic event during the course of their disease, although the reason(s) a thrombotic event may suddenly occur remains an enigma<sup>7,8,9</sup>. Platelet activation, complement-mediated hemolysis, impaired nitric oxide (NO) bioavailability, impairment of the fibrinolytic system, and inflammatory mediators are all proposed mechanisms and thought to be responsible for the increased thrombotic risk in patients with PNH. Multiple factors are likely to contribute to any one thrombotic event in patients with PNH. 10 Therapeutic strategies include terminal complement blockade and bone marrow transplantation. Eculizumab, a monoclonal antibody complement inhibitor, is highly effective and the only licensed therapy for PNH.<sup>11</sup> The therapeutic anti-C5 antibody eculizumab (Soliris, Alexion) has proven effective in controlling intravascular hemolysis *in vivo*, leading to remarkable clinical benefit in a majority of PNH patients.<sup>12,13</sup> Yet, persistent C3 activation occurring during eculizumab treatment may lead to progressive deposition of C3 fragments on affected erythrocytes and subsequent C3-mediated extravascular hemolysis, possibly limiting the hematologic benefit of anti-C5 treatment.<sup>14,15</sup> Thus, upstream inhibition of the complement cascade seems an appropriate strategy to improve the results of current complement-targeted treatment.<sup>16,17</sup>

<https://doi.org/10.1016/j.htct.2022.09.1195>

## Sp11

### HOW WE (WILL) TREAT PNH?

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Clinical signs arising from intravascular hemolysis, hemolysis-related transfusions and thrombosis are indications for treatment initiation in paroxysmal nocturnal hemoglobinuria (PNH), whereas clone size *per se* is not. Eculizumab prevents intravascular hemolysis and reduces significantly thromboembolic risk resulting in a five-year overall survival of >90%.

Hemoglobin value, LDH and reticulocyte count are used to define treatment response. Residual intravascular hemolysis is mainly caused by an incomplete C5 blockage and can lead to continuous low-grade hemolysis or transient breakthrough hemolysis episodes in 10-15% of PNH patients. Additional complement-amplifying conditions such as infections, surgery or pregnancy may overcome efficient therapeutic levels of Eculizumab and therefore require dose adjustments. C3-mediated extra-vascular hemolysis represents the main reason for residual anemia during anti-C5 treatment. Patients with an inherited C5-variant lack response to Eculizumab and have been directed (in past) towards allogeneic HSCT. Transplantation has an overall mortality of up to 30%, with a higher risk in patients with previous thrombosis. A plethora of novel therapeutic agents are reported to impact on both; residual intravascular hemolysis and C3-mediated extra-vascular hemolysis. The new C5 inhibitor Ravalizumab with an eight-week *i.v.* dosing interval showed non-inferiority to Eculizumab. Crovalimab, binding on the single missense C5 heterozygous mutation is injected *s.c.* monthly; two large phase III trials are ongoing as add-on- and mono-therapy. Others, such as Pozelimab, injected subcutaneously on a weekly basis after an initial IV loading dose or Tesidolumab are still under current investigation. Currently investigated proximal inhibitors are acting towards: (i) the C3 complement; (ii) complement factor D or (iii) the complement factor B. They are aiming in particular to prevent C3-mediated extra-vascular hemolysis. Pegcetacoplan is a PEGylated version of compstatin which binds to C3 and is injected *s.c.* in monotherapy 4 weeks after initial concomitant therapy with Eculizumab. In a recent phase III trial, pegcetacoplan showed superiority to eculizumab in hemoglobin change from baseline and is now approved by the FDA for patients with PNH who are either treatment-naïve or switching from anti-C5 monoclonal antibodies. Danicopan is an oral first-in-class factor D complement alternative pathway inhibitor and decreased significantly transfusion requirement, as shown in a phase II trial (phase III ongoing). BCX9930, another FD inhibitor in early development is given orally and demonstrated initial clinical efficacy both as add-on therapy in patients with inadequate response to eculizumab as well as in monotherapy in treatment-naïve patients. In conclusion, novel proximal and distal complement inhibitors with different application modalities, in part as add-on or monotherapy seem to improve significantly intra- and extra-vascular hemolysis in PNH, resulting in a better hematological benefit. Before choosing specific treatment, hematologists have to assess hemolysis, thrombosis and patients' bone marrow function. Future studies will help to explore long-term efficacy and safety of these novel agents.

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## Sp12

### THE THEN, NOW, & FUTURE OF ENGINEERED T-CELL THERAPEUTICS FOR HUMAN APPLICATION

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Since the 1990's, we have conducted clinical trials of gene modified T cells. Chimeric antigen receptor (CAR) T cells independent of HLA and targeting CD19 on B cells leukemias and lymphomas have induced durable complete responses in patients who are relapsed or refractory to all other available treatments. New designs for genetically modified T cells include switches and potency enhancements that will be required for targeting solid tumors. In one such approach, a decoy receptor is inserted into CAR T cells to thwart a tumor immunosuppressive mechanism. Another improvement shortens ex vivo manufacturing, along with the addition of an anti-tumor cytokine to increase in vivo potency. Determining the critical quality attributes, dose, potency, and anticipating pharmacokinetics of a living, dividing drug presents unique challenges. Improving patient access to advanced cell and gene therapies entails not only on scientific progress in targeting, gene modification and cellular manipulation, but also on meeting automation, engineering, clinical site onboarding, and health policy challenges.

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### Sp13

#### FROM ALLOGENIC TRANSPLANTATION TO PRECISION IMMUNE THERAPY

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Allogeneic stem cell transplantation (ASCT) represents a model for immune cellular therapy leading to Immune Precision Medicine. *The pioneers* Georges Mathé in Paris and E. Donall Thomas (Nobel Prize in 1990) in Cooperstown, New York, pioneered ASCCT in the clinical field. In 1958, the first 4 survivors were seen in patients after accidental exposure to lethal or near lethal dose of TBI, in Paris. However, they were subsequently shown to have autologous recovery. Understanding of ABMT immune support begun in 1954 with 1980 Nobel Prize Jean Dausset. The first ABMTs were performed in severe combined immunodeficiencies with the first success observed in 1968 (syngeneic donor), followed in 1973 by unrelated donor ABMT in London. This was also the time of the initiation of registries. *Development time in hematological malignancies* The first success of ABMT in acute leukemia was observed in 1976 in Seattle with a related donor and in 1976 with an unrelated donor. Thereafter, the evolution will take place within the framework of the risk-benefit balance with reduction of the intensity of the conditioning regimen, the graft versus leukemia (GVL)/graft versus host disease (GVH) balance and the donor extension with umbilical cord blood and more recently the haplo-identical allogeneic ASTC. Autologous SCT was introduced at the beginning of the 80s to amplify reduction in tumor mass, particularly in lymphoid malignancies. *Stem cell transplantation as an immune therapy platform* Whatever the autologous or allogeneic context, the

hematopoietic SCT is an exceptional platform for combining, modulating immunotherapy. In an allogeneic context, by modifying lymphocyte subpopulations, such as the supply of cytotoxic T-cells, the modulation of Tregs, the addition or activation of NK cells have an impact on GVH/GVL balance. The enhancement of anti-tumor cytotoxicity can be brought about using monoclonal antibodies (moAb), the addition of cancer vaccines. In an autologous context, there are some windows of opportunity, in the aplasia period due to the accessibility to stressed cancer cells, and cytokine burst approximately at D15, to add cell-drugs such as NK,  $\gamma\delta$  T-cells or anti-cancer moAbs, or to associate chimeric antigen receptor (CAR) immune cells such as CAR-NK, as well as immune checkpoint inhibitors depending on the risks. This paves the way for a real dynamic personalized medicine and should cause the methodology for developing these therapeutic strategies to be rethought. Obtaining an optimization of the clinical efficiency which must be preceded by a reflection of biological efficiency can be helped by mathematical models or AI. We have thus developed a mathematical model for the optimization of the use of anti-IL-6. There is a modeling of use of cytotoxic cells. In cellular therapy, the concept of cell-drugs orients towards non-MHC dependent allogeneic cells such as NK and  $\gamma\delta$  T-cells, as well as obtaining them in large batches to reduce production costs. We are entering a new medical era, with new notions such as dynamic, globalized vision, the use of new tools resulting from the digital revolution, new targeted therapies, immunotherapy, the combination of strategies for better efficiency: the Immune Precision Medicine.

<https://doi.org/10.1016/j.htct.2022.09.1198>

### Sp14

#### EUROPEAN EXPERIENCE FROM BARCELONA – IN-HOUSE PREPARATION AND CLINICAL RESULTS

#### XIII EHO 2022 / CELLULAR THERAPY: CAR T-CELLS IN HEMATOLOGICAL MALIGNANCIES

Manel Juan & a team of more than 200 professional

*Servei d'Immunologia. Hospital Clínic de Barcelona (HCB). Plataforma de Hospital Sant Joan de Déu-HCB. Barcelona – Spain*

ARI-0001 [systematically named Varnimcabtogene autoleucel (var-cel), a second generation anti-CD19 chimeric antigen receptor (CAR) T-cell] granted local use authorization (under the rule of "hospital exemption", HE) by the AEMPS (Spanish drug agency = Agencia Española de Medicamentos y Productos Sanitarios) and just a little more than half-year ago (December 2021) PRIME (Priority Medicine) designation by the EMA (European Medicines Agency) for patients >25 years old with relapsed or refractory (R/R) B cell acute lymphoblastic leukaemia (B-ALL). The authorization is based on the results of a phase 1 clinical trial (NCT03144583), but additional patients (already reimbursed by Spanish Health System), new clinical trials or compassionate uses with ARI-0001, have been produced and infused in our Hospital Clínic de Barcelona or our

pediatric partner, Hospital Sant Joan de Déu. Although HE for adult ALL patients and compassionate uses (next to indicated commercial products that authorized our center) allow us to use CART19 therapy for treating our patients (our real aim of this development), the good clinical results, and petitions of different centers all around the world (specially from places where commercial products are not available) encouraged us to consider how we should proceed to extend our product to other patients. Our Academic proposal is the result of the work of a multidisciplinary team, a point-of-care (PoC) procedure based on a well establish protocol in a commercially available bioreactor and our home-developed lentivirus. All the elements of our proposal follow the GMP standards, strictly controlled by the AEMPS and the regulations for Advanced Therapy Medicinal Products (ATMPs) of the EMA; although the product could be developed in our clean-rooms at Barcelona, our aim is to share procedures to allow production as a real PoC product, looking for partners that can reproduce all steps next to the patient. This multi-site cell production has been already accomplished with success in several clinical trials, while for a homogeneous lentiviral production, we decided (by now) to use facilities centralized in our university hospital. We expect to obtain first local authorization for this multicenter production in Spain, and later by EMA and other regulators (India). In fact, this experience is also supported by developing a clinical trial with 60 multiple myeloma patients under the treatment of a new own CART-BCMA (ARI-0002h). We are convinced that it is a possible model, although most of the huge number of rules are mainly thought for pharma-companies and are not easily implemented by Academic entities. But if we want to have the best treatments for our patients, to find solutions with real options for Academic ATMPs developments is the only way to arrive where the commercial companies, the health systems and in general countries will not be able to arrive for different reasons (difficult recover of investments by complex reimbursement, low level of patients, no-sustainable expenses and procedures for economic and ecologic reason, ...).

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## Sp15

### USA EXPERIENCE: IN-HOUSE PREPARATION: PROSPECTS AND PROBLEMS

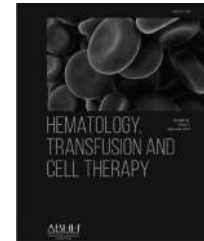
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Adoptive Cellular Therapy (ACT) is transitioning from experimental to standard of care. Limited specificities of chimeric antigen receptor T cells (CAR-T) are licensed drugs, with commercial products selling for ~400,000 USD. Tumor infiltrating lymphocytes (TIL) can target multiple cell surface and intracellular tumor antigens. TIL have not been commercialized, due to complex logistics and cost. Our objective is to leverage a single standardized platform (Miltenyi Prodigy) for in-house ACT. We currently manufacture CD19 CAR-T under an FDA IND and are developing a virtually identical TIL protocol minus the lentiviral vector. TIL are manufactured from malignant pleural effusions rich in immune infiltrates. CD4+ and CD8+ cells are enriched and activated with anti-CD3/CD28 beads. CAR-T are transduced, and both CAR-T and TIL are expanded (IL-7/IL-15) for 5 days. The product is infused fresh, avoiding losses associated with cryopreservation and thawing. Developing and validating release tests (absence of replication competent virus, vector copy number, chimeric antigen receptor expression, endotoxin testing) posed an initial challenge. Having completed assay development, our manufacturing process, including release testing, can be performed for less than 1/10 the cost of commercial CAR-T. We expect that the platform that we have validated will be easily transitioned to new chimeric antigen receptor designs and specificities and will likewise be adaptable to TIL manufacture for the wide variety of cancers that metastasize to the pleura of peritoneum. Standardized in-house ACT manufacture may greatly reduce the cost of cellular immunotherapies, making it more widely available to patients.

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## PEDIATRIC PRESENTATIONS

### Sp01

#### TREATMENT OF SICKLE CELL ANEMIA

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Sickle cell disease (SCD) is an inherited disorder prevalent in many areas of the world including Africa, Middle East and parts of India. It is characterized by repetitive episodes of vaso-occlusive (VOC) process, leading to recurrent painful episodes, hemolytic anemia and predisposition to infection. Although VOC is a leading manifestation of SCD, and seen in about 90% of all patients with SCD, however organ specific complications such as acute chest syndrome, stroke, splenic sequestration, and many skeletal complications are also seen. Better understanding of pathophysiology of the disease as well as worldwide interest in the disease has allowed more progress on treatment and prevention of these complications and development of more focused pharmacological therapies. Hemoglobin polymerization is a primary triggering event in the pathophysiology of the disease, resulting in vascular injury and leading to the process of sickling. This usually ignite an intense inflammatory process/ tissue ischemia and increased adhesions. This understanding of the pathophysiology has allowed scientist to develop drugs (three FDA approved within the last few years), that interfere with these processes such as Voxelotor & Hydroxyurea (interfere with polymerization and enhance HbF production), L-glutamine and Omega 3 (interfere with inflammatory process and oxidative stress) and Crizanlizumab and Tinzaparin (works by inhibiting adhesion molecules). Others studies looking at similar and other pathways are ongoing, including drugs that improve adenosine triphosphate (ATP) levels and reducing 2,3-diphosphoglycerate (2,3-DPG) levels. The availability of these therapeutic interventions, will allow patients and physicians the freedom to have patient specific therapeutic interventions including development of combinations protocols. SCD is very complex and this meant that drug with multi-faceted action such as Hydroxyurea will remain

with us for some time. Further progress also made in the area of bone marrow transplant (including alternative donor pool) and gene therapy /gene editing, with recently published data is very encouraging. Although the prognosis of patients with SCD has improved, due to introduction of vaccination, use of antibiotics prophylaxis and blood transfusions, however still patients are dying prematurely and further work is needed on understanding disease and its manifestation.

<https://doi.org/10.1016/j.htct.2022.09.1202>

### Sp02

#### EARLY T-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDHOOD

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Early T-cell precursor (ETP) ALL accounts for 10% to 15% of T-ALL, which arises from an early T-cell lineage clone with aberrant expression of myeloid and/or early progenitor cell markers (1,2). ETPs are a subset of thymocytes representing recent immigrants from the bone marrow to the thymus, they retain multilineage differentiation potential, suggesting their direct derivation from hematopoietic stem cells (3). ETP-ALL, which was first reported by Coustan-Smith in 2009, largely overlaps with the pro-T subtype of the EGIL classification; its special diagnostic criteria in immunophenotypic screening are the absence of CD1a and CD8 expression, the absence or weak expression of CD5, and the presence of strong positive for at least one of CD34, CD117, HLADR, CD13, CD33, CD11b, and CD65 (2,4-6). In case of strong positivity of CD5, at least two of the latter must be strong positive (6). There is also novel evidence that the myeloid marker CD371 may be positive in ETP (6). The genetic features of ETP-ALL are similar to those of hematopoietic stem cells and myeloid progenitor cells. The genomic mutations of ETP-ALL are enriched in hematopoietic transcriptional regulators (such as BCL11B, ETV6, RUNX1, biallelic WT1, and GATA3), epigenetic factors

(such as histone modification, including PHF6, CTCF, EED, EZH2, SUZ12, and SETD2), and signaling genes (such as activation JAK-STAT, IL-7R and RAS signaling pathway, including JAK1, JAK3, IL7R, SH2B3, NRAS, KRAS, FLT3, NF1, and PTPN11). ETP-ALL has a lower frequency of classical T-ALL genetic alterations such as NOTCH1/FBXW7/CDKN2A mutations and a higher prevalence of FLT3, NRAS/KRAS, DNMT3A, IDH1, IDH2, JAK3, and ETV6 mutations (1,2,5). ETP-ALL was initially thought to have a poor prognosis, but the opinions on it vary (2,3,7). ETP ALL is often corticosteroid resistant and a high percentage of ETP ALL patients have detectable MRD at day 29 including many induction failures (1,2,7,8). No difference in OS was observed in the COG AALL0434 study and UKALL 2003 trial between the patients with ETP-ALL and typical T-ALL (4,9). Therefore, it is important to continue with conventional therapy in ETP-ALL patients who have poor end-induction response; MRD based therapeutic approach is recommended (7,10). Patients with ETP-ALL had high risk of hematological relapse treated at St Jude Children's Research Hospital (3). For relapsed and refractory patients, the use of acute myeloid leukemia-oriented therapies such as FLAG-IDA regimen or targeted agents may be of benefit for some patients, including FLT3 inhibitors, tyrosine kinase inhibitors, BCL-2 inhibitors such as venetoclax, or JAK/STAT inhibitors in patients with JAK mutations or fusions (1,2,4,5,7).

<https://doi.org/10.1016/j.htct.2022.09.1203>

### Sp03

#### SUBCUTANEOUS TREATMENT MODALITIES IN HEMOPHILIA CARE IN 2022

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Hemophilia is a rare hereditary, recessive X-linked, hemorrhagic disorder characterized by deficiency of coagulation factor VIII (hemophilia A) or IX (hemophilia B). A typical presentation of this disease is spontaneous or traumatic bleeding. Although bleeding can occur in any part of the body, the most frequently affected parts are the joints and muscles. Bleeding into the joints (hemarthrosis) can lead to stiffness, pain, swelling and severe joint damage which can cause the patient severe long-term disability and potentially death if untreated. A while ago, **prophylaxis with factor concentrates** started at an early age in children with severe or moderate hemophilia, has proven its efficacy over **on demand treatment** in minimizing the hemorrhagic risk and so the long-term sequelae. Subsequently, after the introduction of **extended half-life factor concentrates**, patients are living longer and "better" as a result of safer factor concentrates, and less treatment burden on young patients. Despite the great efforts of clinical research, until recently there were no treatments other than replacement factors. Lately, "**non-factor therapies**" gained their place in the treatment armamentarium of hemophilia. Those are medications that improve hemostasis without replacing the missing factor. These therapies are all

designed to be given **subcutaneously** and at relatively **infrequent intervals** and thus reducing the treatment burden. The aim of our presentation is to shed the light on different families of "non-factor therapies": **bispecific monoclonal antibody** like **emicizumab** (approved and available to clinicians for the subcutaneous treatment of hemophilia A) and **MIM8** (under investigation), **rebalancing agents** like **fitusiran (an antithrombin inhibitor)** and the **anti-TFPI** (Tissue Factor Pathway Inhibitor) antibodies, as **marstacimab or concizumab**.

<https://doi.org/10.1016/j.htct.2022.09.1204>

### Sp04

#### STEM CELL TRANSPLANTATION IN BRAIN TUMORS

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Central nervous system (CNS) tumors are the second most common pediatric malignancies after acute leukemias and are the most common pediatric solid tumors. Although cure rates have improved with numerous technical advances in multimodal therapy, the prognosis remains poor for some high-risk histological type and for patients with residual, recurrent or disseminated disease. Radiotherapy (RT) remains an integral part of treatment for childhood brain tumors; however, the profound and irreversible sequelae of brain irradiation in the younger children are now well documented. In an effort to decrease irradiation toxicity while improving survival and quality of life in these patients, high-dose chemotherapy with autologous hematopoietic stem cell transplantation (HD-CT&autoHSCT) has been incorporated in both up-front as well as recurrent therapies. In up-front treatment, it is used in patients under the age of 3 years to delay RT or not to use RT at all. It can be used tandem non-myeloablatively in patients older than 3 years of age, after dose-intensive chemotherapy, both to shorten the neutropenic period and to give more intense chemotherapy in a shorter time when compared to conventional chemotherapy treatment approaches. AutoHSCT may also be considered after a myeloablative conditioning regimen for relapsed embryonal brain tumors, as either once or tandem, in cases with good response to salvage therapy as consolidation. In this talk, the role of autoHSCT in childhood brain tumors will be discussed by giving the results from international studies.

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### Sp05

#### TREATMENT/MANAGEMENT OF OTHER HEPATIC TUMORS

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Pediatric liver neoplasias are rare, comprising 1–4% of all solid childhood tumors. More than half of these masses are due to hepatoblastoma and hepatocellular carcinomas, making remaining various liver tumors much more rarer. *Hepatic mesenchymal hamartoma (HMH)* is a benign tumor observed in children less than five-year-old. It is located in the right lobe of the liver more often. It has a cystic structure, and AFP is generally normal or slightly elevated. The treatment is complete resection. In rare cases, HMH can transform into undifferentiated embryonal sarcoma. *Focal nodular hyperplasia* is a well-circumscribed benign lesion, which is usually discovered incidentally as well as with oral contraceptive use, postchemotherapy status, and hereditary hemorrhagic telangiectasia. Typical imaging finding is a central scar in the mass lesion, which might overlap with fibrolamellar hepatocellular carcinoma. Asymptomatic cases might be managed with an expectant approach by careful monitoring whereas symptomatic cases might be treated with surgery or ablation therapy. *Infantile hemangioma* is the most common benign hepatic tumor in infancy. Symptoms at admission may include abdominal distention due to hepatomegaly, congestive heart failure, feeding problems, anemia, thrombocytopenia and consumptive coagulopathy, jaundice. Many of these hemangiomas are discovered incidentally and are localized. In most cases, these lesions are small enough to be of no clinical significance. In severe cases, propranolol, corticosteroids, mTOR inhibitors or cytotoxic agents can be used for treatment. *Undifferentiated embryonal sarcoma of the liver (UESL)* is the third most common malignant liver tumor in children. The median

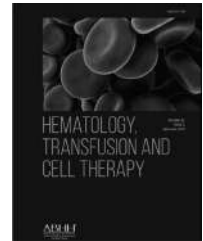
age of diagnosis of UESL is 10,5 years, in comparison to that of liver rhabdomyosarcoma which is 3.6 years. UESL is an aggressive malignancy that should be treated with multimodal therapy. Most important prognostic factor is the completeness of the resection. The survival is reported to range between 70% and 90% in various case series. *Rhabdomyosarcomas* are observed in the biliary tract. The usual sign in admission is obstructive jaundice with or without abdominal mass. Treatment is multimodal therapy. With CWS protocols, the 5-year overall (OS) and event free survival (EFS) rates were 58% and 47%, respectively. *Hepatic angiosarcoma* is a rare but highly aggressive malignancy of endothelial cells, previously known as infantile hemangioendothelioma type 2. There is a girl predominance. Despite multi-agent aggressive treatment approaches including liver transplantation, the overall prognosis is still poor.

**Table-1-Distribution of primary liver tumors of children\***

Age group	Malignant	Benign
Infants, toddlers	Hepatoblastoma (43%)	Hemangioma/vascular (14%)
	Rhabdoid tumor (<1%)	Mesenchymal hamartoma (6%)
	Malignant germ cell (<1%)	Teratoma (<1%)
School age, adolescents	Hepatocellular and transitional cell tumors (23%)	Hepatic adenoma (2%)
	Sarcomas (7%)	Focal nodular hyperplasia (2%)

\* Von Schweinitz D.: Management of liver tumors in childhood. Seminar in Pediatric Surgery 2006; 15: pp. 17-24.

<https://doi.org/10.1016/j.htct.2022.09.1206>



## ORAL PRESENTATIONS

### ADULT HEMATOLOGY ABSTRACT CATEGORIES

#### ACUTE LEUKEMIA

##### OP 01

#### THE ACUTE LYMPHOBLASTIC LEUKEMIA OF DOWN SYNDROME

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**Objective:** Down syndrome (DS) is a genetic disorder caused by the presence of a third copy of chromosome 21. It is usually associated with physical growth delays, mild to moderate intellectual disability, and characteristic facial features. Children with DS are at an elevated risk of leukemia, especially myeloid leukemia. On the other hand, children with DS are at a 20-fold increased risk for acute lymphoblastic leukemia (ALL). In our case, we presented a patient with DS who was diagnosed with ALL. **Case report:** 19-year-old male was admitted to the emergency department due to abdominal pain. On his physical examination, splenomegaly was detected. In laboratory examinations; kidney and liver function tests were normal, lactate dehydrogenase: 372 U/L, uric acid: 5.4 mg/dl, white blood cell:  $25000 \times 10^6/L$ , lymphocyte:  $15780 \times 10^6/L$ , neutrophil:  $1140 \times 10^6/L$ , hemoglobin: 10 gr/dl, thrombocyte:  $12000 \times 10^6/L$ , coagulation tests were normal and in peripheral blood smear evaluation, 90% blast cells were detected. **Methodology:** Peripheral blood flow cytometry evaluation was compatible with B-ALL (TdT, CD19, CD10, CD34, cCD79a, CD58, CD9, CD38, CD123, CD20, CD81, CD22 positivity in atypical cells). Bone marrow biopsy was hypercellular. There was diffuse blastic cell infiltration, which stained extensively with TdT, CD79a. Chromosomal analysis is 47XY,+21 and t(12,21)(p13.2;q22.12) (ETV6/RUNX1) (FISH) and 14q32.33 (IGH) FISH were positive, t(9;22) P190 -p210, t(4;11), t(1;19), 11q23 were negative. The risk classification was standard risk. **Results:** AUGMENTED BFM induction chemotherapy protocol was started. Pancreatitis was developed after peg-asparaginase

and chemotherapy-related hepatotoxicity (grade 1) was developed. Central nervous system prophylaxis (intrathecal methotrexate) was applied. The control bone marrow biopsy performed after induction was normocellular, the blast rate was <5%. BFM standard risk first consolidation chemotherapy protocol was started. He died of septic shock on the eighteenth day of the first consolidation treatment. **Conclusion:** Cases of DS-ALL cases are at greater risk for serious side effects from chemotherapeutics, mortality and recurrence than non DS-ALL. Because children with DS have a higher incidence of treatment-related toxicity, survival rates are lower than non-DS children. During ALL induction chemotherapy life-threatening side effects are tumor lysis syndrome, thrombosis, bleeding and infection. In the UKALL 2003 study, DS associated with a significantly increased risk of death from sepsis during chemotherapy.

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#### LYMPHOMA

##### OP 02

#### LOW INCIDENCE OF CENTRAL NERVOUS SYSTEM (CNS) RELAPSE OF DIFFUSE LARGE B-CELL LYMPHOMA DESPITE LIMITED USE OF INTRATHECAL PROPHYLAXIS

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**Objective:** Diffuse large B cell lymphoma (DLBCL) is the commonest sub type of non-Hodgkin's lymphoma (NHL) accounting for 30–50 % of NHL cases. Around 2% to 10% of patients with diffuse large B-cell lymphoma (DLBCL) experience central nervous system (CNS) relapse after initial therapy which

is associated with a poor prognosis and most often a fatal outcome. The incidence of CNS relapse can vary from <1% in younger, good-risk patients, to around 30% in patients with multiple risk factors, however, the relapse risk was reported to be lower in the rituximab era in some studies. Moreover, optimal modality of CNS prophylaxis remains to be defined, with both systemic and intrathecal (IT) chemotherapy being widely used. As the incidence of CNS relapse and type of prophylaxis used varies in different reports, it is important to study this risk in different populations to implement optimal prophylaxis strategies. The Objectives of this study was to evaluate the incidence of CNS relapse in DLBCL patients at our institution and to study risk factors and the type and role of CNS prophylaxis. **Methodology:** We retrospectively analyzed patients diagnosed with DLBCL at King Khalid University Hospital, Riyadh, from January 2011 to June 2019. Data were collected from computerized hospital information system and from the files of the patients. Variables studied included age at diagnosis, stage at diagnosis, international prognostic index (IPI) and CNS-IPI score, site(s) of extra-nodal involvement, type of chemotherapy received, CNS prophylaxis and CNS relapse. CNS prophylaxis was administered on the basis of presence of high-risk features like presence of  $\geq 2$  extranodal sites, involvement of bone marrow, bone, testes, nasopharynx and paranasal sinuses. Patients with presence of CNS involvement at diagnosis and primary CNS lymphoma were excluded. **Results:** A total of 101 patients were diagnosed with DLBCL during the study period. There were 58 males and 43 females with a median age of 56 (range: 16-87) years. Ann Arbor stage of I-IV was assigned in 9, 21, 17 and 50 patients, respectively. The lung was the most common extranodal site involved in 27 (26.7%) patients, and liver and bone marrow involved in 20 (19.8%) patients each. Gastrointestinal tract was involved in 9 (8.9%) patients, kidneys in 5 (4.95%), breast in 4 (4%), and testis and adrenal in 2 (2%) patients each. Twenty-five (24.75%) patients had high risk CNS-IPI score, 44 (43.5%) had intermediate risk score and 32 (31.7%) had low risk score. Ninety-four (93%) patients received R-CHOP chemotherapy while rest of the patients received other types of chemotherapy, mostly a milder regimen (R-CVP), because of comorbidities and poor performance status. Sixteen patients received CNS prophylaxis, which was IT methotrexate (MTX)  $\pm$  cytarabine/hydrocortisone in all patients. Nine of 25 (36%) patients with high-risk CNS-IPI score did not receive CNS prophylaxis. After a median follow up of 36 months (range 4-114), 2 (2%) patients developed CNS relapse and died shortly after this diagnosis. Both the patients with CNS relapse had high risk CNS-IPI score and did not receive CNS prophylaxis. **Conclusion:** CNS relapse of DLBCL was uncommon in this patient population despite limited use of IT CNS prophylaxis in high-risk patients. Low incidence of CNS relapse in many high-risk patients despite limited use of IT prophylaxis may be related to rituximab use and/or other factors. Our data indicate that IT CNS prophylaxis may be adequate for DLBCL patients at high risk of CNS relapse.

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## OP 03

### AN UPDATED OF PIONEER PROJECT TO COLLECT DATA OF T-CELL NHL PATIENTS AMONG FIVE REGIONS OF BRAZIL. T-CELL BRAZIL PROJECT

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**Objective:** T-cell Brazil project started in April 2017 an ambispective study focusing to collecting epidemiological and clinical data from the most frequent subtypes of PTCL. Our goals are to obtain the frequency of subtypes by the five Brazilian macro regions; to investigate the clinical and biology characteristic; to create a routine pathological revision and to evaluate the OS, EFS in 5 years of follow-up. **Methodology:** Thirteen nine centers had approved by their Ethical Committee and using REDcap Platform by Vanderbilt are registering their cases. Descriptive and bivariate analyses, then it was applied Kaplan-Meier method and log-rank test to obtain survival estimates, using IBM-SPSS v.24 **Results:** The median age was 55 years (19-95); 56% male; Almost 72% had advanced stages, 28% ECOG  $\geq 2$ ; the distribution of main subtypes was: 31% PTCL-NOS; 18% ALCL, ALK-; 16% ATL; 13% ENKTL nasal and nasal type; 11% AITL; 7% ALCL, ALK+; 6% others (Table 1). 50% of patients were alive and the 24-month PFS and OS was 36% and 50%, respectively. OS by main subtypes was 48% PTCL-NOS; 61% ALCL, ALK-; 33% ATL; 46% ENKTL nasal/nasal type; 48% AITL; 80% ALCL, ALK+. **Conclusion:** This is the first experience cover all over the country, focusing also an educational and of interchanging experience network among the multidisciplinary health team in Brazil. The target of 500 was exceeded; however, the registry will go on until December as planned. All cases have been reviewed both in the registry and by pathologist Committee, and we esteem some cases



will be excluded for different reasons and anyway it will help for future analyses if the number of registers is higher.

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## MYELOMA

### OP 04

#### UPDATED PROGRESSION-FREE SURVIVAL (PFS) AND DEPTH OF RESPONSE IN IKEMA, A RANDOMIZED PHASE 3 TRIAL OF ISATUXIMAB, CARFILZOMIB AND DEXAMETHASONE (ISA-KD) VS KD IN RELAPSED MULTIPLE MYELOMA (MM)

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**Objective:** The anti-CD38 antibody Isa in combination with Kd is approved in various countries for patients (pts) with relapsed MM after  $\geq 1$  prior therapy, based on primary interim analysis (IA) of the Phase 3 IKEMA study (NCT03275285). Here we report updated efficacy and safety Results from IKEMA. **Methodology:** This prespecified final analysis (Isa-Kd 179, Kd 123 pts) evaluated updated PFS (primary endpoint), PFS2, CR rate, MRD- rate,

and MRD- and CR rate in ITT population, and safety with 2 additional years of follow-up. Isa 10mg/kg was given IV qw for 4 wks and then q2w; Kd 20/56mg/m<sup>2</sup> biw, 3/4 weeks. Hydrashift Isa IF assay was used to rule out potential Isa interference in CR determination. At cutoff (14Jan2022; median follow-up 44 mo), 49 (27.4%) Isa-Kd, 11 (8.9%) Kd pts were still on treatment. **Results:** Updated PFS was consistent with primary IA Results, showing significant benefit of Isa-Kd (vs Kd): PFS HR 0.58; PFS2 HR 0.68. Final CR rate (Isa-Kd vs Kd) was 44.1% vs 28.5%, MRD- rate 33.5% vs 15.4%, MRD- and CR rate 26.3% vs 12.2% (**Table**). Serious TEAEs were reported in 70.1% Isa-Kd vs 59.8% Kd pts. The most common, any-grade non-hematologic TEAEs in Isa-Kd were infusion reactions (45.8%), diarrhea (39.5%), hypertension (37.9%) and upper respiratory tract infection (37.3%). **Conclusion:** These Results show unprecedented mPFS, CR rate, MRD- and MRD- CR rates in a non-lenalidomide containing regimen with benefit maintained through subsequent therapies and a manageable safety profile. Safety profiles and efficacy Results in both arms were consistent with prior IKEMA findings. Our findings support Isa-Kd as a standard of care treatment for pts with relapsed MM.

	Isa-Kd n=179	Kd	
Median PFS, months	35.7 (28.8-44.0)	19.2 (15.8-25.0)	HR (95.4% CI) 0.58 (0.42-0.79)
Median, PFS2, months	47.2 (38.1-NC)	35.6 (34.0-40.5)	HR (95% CI) 0.68 (0.50-0.94)
	n (%) 95% CI	n (%) 95% CI	odds ratio 95% CI
ORR	155 (86.6) 0.81-0.91	103 (83.7) 0.76-0.90	-
CR	79 (44.1) 0.37-0.52	35 (28.5) 0.21-0.37	2.09 1.26-3.48
MRD-rate	60 (33.5) 0.27-0.41	19 (15.4) 0.10-0.23	2.78 1.55-4.99
MRD and CR rate	47 (26.3) 0.20-0.33	15 (12.2) 0.07-0.19	2.57 1.35-4.88
Table: Efficacy (ITT) CI confidence interval, HR hazard ratio, ITT intent to treat, NC not calculable, ORR overall response rate			

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## STEM CELL TRANSPLANT

### OP 05

#### PEDIATRIC ACUTE MYELOID LEUKEMIA (AML): NOTCH1 ACTIVATION INFLUENCING PROGNOSIS THROUGH TRANSFORMING GROWTH FACTOR-B (TGF-BETA) / SETBP1; REPORT OF A PILOT STUDY FROM SAUDI ARABIA

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**Objective:** NOTCH1 is now established to play a key role in the prognosis of several hematological malignancies. Notch proteins are multifaceted and involved in several key cellular functions with extensive crosstalk with other critical pathways; therefore, it is important to investigate NOTCH1 expression and its influence on other oncogenic pathways molecules in AML. In this pilot study, we correlated NOTCH1 and associated pathway expression patterns among childhood AML patients and correlated it with hematological parameters and overall survival (OS) data. **Methodology:** RNA from diagnostic BM biopsies (n=35) were subjected to expression analysis employing nCounter Pan-Cancer pathway panel by Nanostring technologies. Laboratory and clinical data were correlated with expression of NOTCH1 and several other oncogenic signaling pathways (n=780). nSolver software v3 and SPSS software v24.0 were utilized for statistical evaluation. Hierarchical clustering and principle component analyses were performed employing QluCore Omics Explorer v3.2. **Results:** 35 -AML patients (median age 8 yrs., range <1-18 yrs.) were dichotomized into low NOTCH1 (17/35; 49%) and high NOTCH1 (18/35; 51%) groups based on receiver operating characteristic (ROC) curve analysis (74% AUC; 82% sensitivity /68% specificity). Age, gender, hematological data or molecular risk factors (FLT3 mutation/molecular fusion) exposed no significant differences across these two distinct NOTCH1 expression groups ( $P > 0.05$ ). High NOTCH1 expression was linked with high expression of NOTCH1 ligand (Dll1) ( $P < 0.001$ /fold  $> 2.5$ ). Our data also showed that high NOTCH1 mRNA is interrelated with heightened expression of positive regulator of the NOTCH signaling pathway (DTX1/DTX3). High NOTCH1 samples also showed high expression of TGRF-b associated protein SETBP1 ( $P < 0.001$ /fold  $> 2.5$ ) (Figure 1A). The level of NOTCH1 expression did not correlate with mortality {5/17 (29%) vs. 6/17; (35%)  $P > 0.05$ }. Low NOTCH1 expressers showed better OS {740 days vs. 579 days; log-rank  $P = < 0.007$ ; HR 6.3 (1.36-29.26)} **Conclusion:** Our pilot study identified high Notch1 expression through canonical pathway as an important poor prognostic marker among pediatric AML patients which is independent of conventional prognostic markers and can provide insights into novel potential therapeutic target. Our study has identified that high expression of the molecules linked with NOTCH1 pathway are an important poor prognostic marker among childhood AML patients. NOTCH1 expression also shows cross talk with several other signal transduction pathways especially TGFb / SETBP1 which are also linked with poor prognosis.

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#### OP 06

##### EVALUATION OF COVID-19 FEAR AND QUALITY OF LIFE IN PATIENTS WITH HEMATOPOIETIC STEM CELL TRANSPLANTATION DURING THE COVID-19 PANDEMIC

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**Objective:** The coronavirus disease 2019 (COVID-19) pandemic has an impact on physical health, but also has effects on mental health. With the COVID-19 pandemic, the level of fear increases and fear triggers many psychological diseases such as depression. We aimed to determine the COVID-19 fear situation in hematopoietic stem cell transplantation (HSCT) patients and to examine its relationship with the quality of life. **Methodology:** In this prospective study, 64 patients who underwent HSCT during the pandemic (between 11 March 2020 and 31 December 2020) were included. The COVID-19 fear situation was evaluated with the Fear of COVID-19 Scale (FCV-19S). Quality of life was evaluated with the European Organization for Quality of Life Research and Treatment Core Questionnaire (EORTC QLQ-C30) (version 3). **Results:** The median FCV-19S score was 16.5 (12.0-22.0). The FCV-19S score was significantly higher in urban residents than rural residents (19.0 (15.0-23.5) vs 14.0 (9.0-22.0) ( $p = 0.44$ )). The general health score was  $59.64 \pm 20.04$ . The strongest positive correlation between fear level and quality of life was found in emotional function ( $r = 0.474$ ,  $p < 0.01$ ). In addition, a weak, significant, positive correlation was observed between role function, nausea-vomiting, pain, anorexia, and fear level. **Conclusion:** FCV-19S is a short, safe and valid tool that can be used to determine the COVID-19 fear level in vulnerable patient groups such as HSCT patients and to direct them to the necessary psycho-oncological support.

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#### OP 07

##### UMBILICAL CORD BLOOD (UCB) AND BONE MARROW (BM) AS A SOURCE OF NATURAL KILLERS (NK) FOR KIR-ALLOREACTIVE ADOPTIVE IMMUNOTHERAPY (KIR-AI)

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**Objective:** NK are innate lymphoid cells with the ability to rapidly recognize and exhibit cytotoxicity toward tumor and virus infected cells in HLA-independent manner without prior activation. KIR-AI is the next promising step after KIR-alloreactive NMAC alloBM transplantation (not only in hematology). We evaluate NK amount, the balance of activating and inhibitory receptors (rp) of different sources, outcomes of KIR-AI UCB/BM. **Methodology:** NK UCB, BM, peripheral blood (PB) were evaluated by flow cytometry (CD3, 7, 16, 56, 94, NKG2A),

KIR by PCR. Mathematical model was developed for evaluation the balance of activating and inhibitory rp as an index of cytotoxic activity (ICA) of mature NK. To select donor (dn) for KIR-AI we investigate med 3 samples (range 3-8) BM/UCB. The indication - salvage therapy, ECOG>3. BM-dn with low ICA were excluded. Lymphodepletion included CyFlu (up to 3 d), both BM (12 pts) and UCB (11 pts). **Results:** NK UCB ranged 5-56% (med 16) of lymphocytes. No any differences between NK-UCB and BM (similar to PB). For dn and pts no ICA differences by sex and age, ICA depend on depression and virus. For pts no ICA difference by type of cancer, germinal mutations, but strong correlation with nearest outcome of cancer. FU med 9 mo (2-52). OS (11 pts, 14 UCB-transfusions) med 6 mo (2+ -10), comparable to BM med 8 mo (2-48). AI outcomes depend on the intensity of lymphodepletion and ICA UCB/BM. **Conclusion:** Considering acceptable toxicity of lymphodepletion and good AI tolerability, including poor pts, the indications for cellular anticancer treatment could be expanded. We start pilot using UCB for KIR-AI for overcome chemoresistance and to achieve complete remission of disease after finishing anticancer treatment of solid tumors and for MRD-eradication in hematology. Additional undeniable advantage of UCB KIR-AI is quick availability of UCB from a KIR-typed UCB register.

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#### OP 08

##### HUMORAL IMMUNITY RESPONSES AFTER VACCINATION FOR HEPATITIS B VIRUS IN AUTOGRAFTED PATIENTS: A SINGLE CENTER EXPERIENCE

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**Objective:** The effectiveness of vaccinations post hematopoietic stem cell transplantation (HSCT), is a reliable marker for immune system's functionality assessment. In autologous HSCT (AHSCT) setting, the general aspect is that the immune system recovers quite soon and patients (pts) are considered to be immunocompetent in a period of approximately 3-6 months post AHSCT. We evaluated the hepatitis B virus (HBV) vaccination responses in autografted pts who were in remission and off chemotherapy post AHSCT. **Methodology:** 27 autografted pts aged 51,6 (22-67) ys, who had antiHbs titers <10 IU/ml before AHSCT and at the time of vaccination, were studied. After a successful engraftment the median absolute

lymphocytes count at +3 months was 1740(450-4090)/mm<sup>3</sup>. In 4,3(0,6–8,5) ys post AHSCT, 3 doses of recombinant HBV vaccine were given monthly. The response rates for pts who completed 3 vaccine doses, compared with an internal group of healthy individuals, vaccinated in the same period with the same product. **Results:** After the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> dose the response rates in the study group were 11%, 81% and 88% respectively. No factor statistically significantly influenced the achievement of protective antiHbs titers. The responses were lower as compared to product's efficacy profile (19%, 86% and 100% after the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> dose respectively), while in the comparative analysis with the internal control group, a trend for inferior responses in autografted pts was also noticed (88% vs 100%, p=0,07). **Conclusion:** This study, in a relatively homogenous group of pts, to our knowledge, is the only one that directly compares the HBV vaccine responses in autografted pts with healthy individuals. Although vaccination was offered late post AHSCT, the responses were lower compared to healthy individuals, indicating a possible long lasting immune impairment post AHSCT highlighting the necessity of prolonged surveillance and intensified vaccination programs for autografted pts.

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#### OP 09

##### ANTIBODY RESPONSES AND SAFETY OF THE COMMERCIALLY AVAILABLE VACCINES AGAINST SARS-COV-2 VIRUS IN ALLOGRAFTED PATIENTS: REAL WORLD DATA FROM A SINGLE CENTER

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**Objective:** Patients (pts) who have undergone allogeneic stem cell transplantation (alloSCT) are at high-risk for life-threatening complications post SARS-CoV-2 infection, and the mortality rates has been reported of approximately 30-35%. The currently available vaccines proved their effectiveness in the general population by reducing the severity of the COVID-19 infection however, scant data exist regarding the safety and efficacy of the commercially available vaccines in allografted pts. **Methodology:** After a median of 2,7 (0,3-6,7) ys post alloSCT, 20 pts received within a median of 42 days, 2 vaccines of either Pfizer (n=17) or combinations of Pfizer with Moderna (n=2) or AstraZeneca (n=1). Off immunosuppression without evidence of active GvHD were 14 pts, 1 was only on Cyclosporine (CSP) while 5 were on steroids plus CSP or MMF or Ibrutinib for GvHD treatment. Automated commercial chemiluminescence immunoassay (CLIA) against spike (S1/

S2) protein was used for antibody responses detection. **Results:** During vaccination program no side effect grade  $\geq 3$  (including allergy, thrombosis, heart dysfunction or laboratory abnormalities) was reported. The commonest complains were fatigue (20%), bony pain (10%) and fever  $<38.5$  oC (10%). Satisfactory antibody responses were observed in 66% and 95% of pts after the 1st and 2nd dose respectively. Importantly, active GvHD and intensive immunosuppression, did not negatively affect the antibody responses. None of the vaccinated pts developed COVID infection **Conclusion:** Our retrospective study although with small number of patients and with short term follow-up, in agreement with others, confirms that the current commercially available vaccines against SARS-CoV-2 are safe and highly effective in producing effective humoral responses in allografted patients. Prospective studies with longer follow-up are needed to elucidate the proper timing and the number of necessary doses for a safe and effective approach in preventing severe COVID-19 infection

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## OTHER DISEASES

### OP 10

#### THE MENTAL HEALTH STATUS OF INPATIENTS WITH NEWLY DIAGNOSED HEMATOLOGICAL CANCER DURING THE COVID-19 PANDEMIC

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**Objective:** There is limited data in the literature on the mental health of newly diagnosed hematological cancer (HC) patients in COVID-19 pandemic. This study evaluates the mental health statuses of HC inpatients diagnosed during the COVID-19 pandemic in comparison to the statuses of patients diagnosed with HC before the pandemic. **Methodology:** A cross-sectional survey collected the mental health measurements of 77 inpatients with HC between March and May 2021. The levels of depression, generalized anxiety, distress, sleep disorder, health anxiety, trait anxiety, coronaphobia, and resilience in HC patients newly diagnosed during the pandemic (NDHC) (n=38) and HC patients diagnosed before the pandemic (BPHC) (n=39) were compared. The relationships between predictive factors and cancer patients' mental health statuses were evaluated. **Results:** Depression (63.2% vs. 35.9%,  $p=0.017$ ) and sleep disorder (67.8% vs. 38.5,  $p=0.016$ ) were significantly higher, while generalized anxiety (57.9% vs. 38.5%,  $p=0.088$ ) and distress (52.6% vs. 33.3%,  $p=0.087$ ) were higher in NDHC. Health anxiety was more common in BPHC (53.8% vs. 31.6%,  $p=0.048$ ). Among NDHC, women had more anxiety

symptoms than men (76.5% vs. 42.9%,  $p=0.037$ ). Diagnosing newly increased the risk of severity of depression and sleep disorders, but decreased the risk of health anxiety. **Conclusion:** Our data indicate that patients with HC are vulnerable to mental health problems in the COVID-19 pandemic. This vulnerability is higher in newly diagnosed HC patients than in patients diagnosed before the pandemic. These findings may help develop interventions that reduce the vulnerability to adverse psychological effects by identifying risk factors for HC patients under pandemic conditions.

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### OP 11

#### CORONAVIRUS ANXIETY LEVEL AND COVID 19 VACCINE ATTITUDE AMONG HEMATOLOGICAL MALIGNANCY PATIENTS

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**Objective:** The COVID-19 vaccine is the most essential tool for altering the pandemic's trajectory. The pandemic's control is complicated by society's unwillingness to vaccination. The aim of this study was to evaluate the attitudes of patients with hematological malignancies towards vaccination and to determine the relationships between vaccination hesitancy and patient characteristics. The secondary aim was to identify the pandemic-related anxiety level of this patient group and to investigate whether anxiety influences vaccination propensity. **Methodology:** This cross-sectional study was conducted with hematological malignancy patients at Hematology Clinic of the Erciyes University Hospital from Kayseri, Turkey, from 1 May 2021 to 1 December 2021. Patients who <sup>(1)</sup> were 18 years old or older, <sup>(2)</sup> voluntarily agreed to take part survey, and <sup>(3)</sup> could understand and perform the questionnaire met the inclusion criteria. 165 patients with hematological malignancies were included. The questionnaire consisted of three parts. The patients' sociodemographic characteristics, such as age, gender, diagnosis, disease and HSCT status, education level, marital status, location of residence were all asked about in the first section of the study. COVID-19 anxiety situation was evaluated with the Coronavirus Anxiety Scale (CAS). COVID-19 vaccine attitude was evaluated with the Vaccine Attitudes Review (VAX) Scale. **Results:** The median age was 48 (18 - 86) years, 61 (37%) of whom were female. Most of the participants (37%) had been diagnosed with acute myeloid leukemia and were undergoing chemotherapy. In addition, 21% of patients reported having comorbidities. At the time of the survey, 70% of patients had not been infected with COVID-19, whereas 44% had been vaccinated. The mean CAS score was 2.42 (0 - 17). There were 22 (13%) participants with a mean CAS score of  $\geq 9$ . Half of the participants had a CAS

score of 0. The CAS score was higher in females ( $p= 0.023$ ). Similarly, it was significantly higher in patients who were not in remission for hematological malignancy and who received active chemotherapy ( $p= 0.010$ ). The mean VAX score was  $49.07 \pm 8.76$  (27-72). Most of the participants (64%) had a neutral attitude towards COVID-19 vaccination. In a survey of 165 patients, 55% said that they were skeptical about vaccination safety, and 58% said that they were concerned about unintended side effects. In addition, 90% expressed moderate concerns about commercial profiteering. Natural immunity was preferred by 30% of the participants. There was no statistically significant correlation between CAS scores and Vaccine Attitudes Review (VAX) Scale. **Conclusion:** This study draws attention to the level of anxiety in patients with hematological malignancies of the COVID-19 pandemic. Negative attitudes towards the COVID-19 vaccine are worrisome for at-risk patient groups. We think that patients with hematological malignancies should be informed to eliminate their hesitations about COVID-19 vaccines.

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#### OP 12

##### TREATMENT OF A PATIENT DIAGNOSED WITH ERDHEIM CHESTER'S DISEASE IN COOPERATION WITH PLASTIC SURGERY AND HEMATOLOGY

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**Objective:** Erdheim Chester disease (ECD) is a rare non-Langerhans histiocytic multisystem disorder. ECD is most commonly manifested as multifocal sclerotic long bone lesions. Orbital and intraocular manifestations are rare. We report an unusual bilateral orbital presentation as xanthomatous infiltration of ECD. **Case report:** A 56-year-old male was admitted due to papular lesions on both eyelids. Eyelid tissue histology showed histiocytic infiltration consistent with ECD. BRAF V600E mutation (-). In the first year, PET-CT showed new lesions on the lymph node, eyelids, knees and elbows. Laboratory investigation was within normal apart of mild increased CRP. The disorder was unresponsive to pegylated interferon alfa. With cladribine of 3 courses and surgical intervention he achieved a nearly normal facial appearance. **Conclusion:** Uncontrolled cell survival, differentiation, and proliferation of histiocytes in ECD result in soft tissue thickening and progressed to chronic fibrotic disease which may be unresponsive to medical treatments and requires surgical interventions.

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#### OP 13

##### A RARE PRESENTATION OF SYSTEMIC AL AMYLOIDOSIS; PULMONARY AL AMYLOIDOSIS

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**Objective:** Involvement of the lung is common in systemic AL amyloidosis in post-mortem series. However, the diagnosis is challenging. Histology is the gold standard but may result in bleeding. Consequently, diagnosis during life is rare. **Case report:** A 58-year-old female was admitted with chest pain, weight loss and cough. Thorax CT showed diffuse ground glass opacities, increased nodular density, and conglomerated mediastinal lymph nodes. Lung biopsy revealed Congo red (+) and anti-amyloid A (-). Bone marrow showed clonal plasma cell increase as 15% of kappa type. No other organ involvement or lytic lesions on PET-CT were documented. Cardiac involvement was detected. Daratumumab-bortezomib-based treatment with doxycycline was started. **Conclusion:** Clinical symptoms and laboratory testing cannot specially confirm the diagnosis of pulmonary amyloidosis. The usual presentation is diffuse-alveolar septal involvement. Diffuse parenchymal involvement is one of the least common forms of respiratory amyloidosis. It should be considered in the differential diagnosis in elderly patients.

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#### PP14

##### REAL-LIFE STUDY OF BIO-CLINICAL FOLLOW-UP AFTER BNT162b2 mRNA COVID-19 (BNTCV) VACCINATION IN 235 PATIENTS (PTS) INCLUDING 225 WITH HEMATOLOGICAL MALIGNANCIES (HM).

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Pts with HM may have low or delayed specific immune response after usual vaccination due to immune deficiency, associated to the disease or to the therapy. In this real-life study, 235 pts vaccinated with BNTCV (BioNTech Pfizer) were monitored for 2 years, starting 06/20 in a single Institution. Patients' population and follow-up. 235 patients including 225 with HM initially received 2 doses of BNTCV (IM) with 3 weeks between the 2 first doses, including 98 lymphomas (L), 28 monoclonal gammopathies with undetermined significance (MGUS), 34 multiple myelomas (MM), 34 myeloproliferative disorders (MPD), 27 chronic lymphocytic leukemias (CLL), 4 acute leukemias and 10 non-malignant hemopathies. The first 43 pts had initial follow-up by telemedicine system connecting the pt to the Institute, developed by La Valeriane Inc. (Montpellier, France), 24/24h, 7 days. Seroconversion was assessed by analyzing IgG anti-Spike protein antibody (AcAS) every 3-4 weeks after the first vaccination and then, every 3-4 months, by SARS-CoV-2 IgG II Quant<sup>®</sup> Assay (Abbott, France) and Elecsys<sup>®</sup> Anti-SARS-CoV-2 S (Roche Diagnostics, France), in duplicate with the 2 assays, by 2 independent labs. Additional boosts of vaccine were administered in case of seronegativity or when the level of antibody was <7 BAU/mL. Pts not seroconverted after 4-5 doses of vaccine received tixagevimab/cilgavimab (EVUSHELD<sup>®</sup>, AstraZeneca). Tolerance using telemedicine application. Local pain (<1 day) was common and transient, particularly after the 2nd dose. 4/43 pts reported significant adverse events through telemedicine, followed by a medical call, including severe asthenia for  $\geq 2$  days, fever (>38°C) for at least 2 days, headache, or general pain. The satisfaction survey of monitoring system was good. Adherence to vaccination was excellent (only one refusal/235 pts). AcAS follow-up 15 Results were discordant (12 with Abbott +, Roche -, and 3 with Abbott - Roche +). Semi-quantitative rapid test (BIOSIS HEALING, Beijing China) was compared to Abbott with good concordance on 97 samples. After 2 doses of BNTCV, 72% of the pts were seroconverted, (median, range) (59, 3-319) BAU/mL, Abbott), including 62% CLL (121), 66% L (39), 91% MGUS (204), 61% MM (15) and 81% SMD (50). 50% of the pts receiving daratumumab (median 8 BAU/mL, 1-20) and only 38% of the pts receiving rituximab (median 0, 0-20) were seroconverted, as compared to 71% of the pts receiving other treatment or 80% (42, 2-210) with no therapy (161, 29-637) ( $p < 0.001$ ). Low gammaglobulin levels (<5g/L,  $p = 0.019$ ), similarly to the IgG level were associated with reduced seroconversion. Median levels of AcAS were 1679 BAU/mL post 2<sup>nd</sup> dose if seroconverted after the 1<sup>st</sup> dose and 308 if seroconverted only post 2<sup>nd</sup> dose. 68% of the pts negative after the 2<sup>nd</sup> dose were positive after the 3<sup>rd</sup> dose. 16 pts received tixagevimab/cilgavimab, 6 having symptomatic non-severe COVID-19 in the 15-40 days after the injection. There is a need to follow AcAS (including with rapid test) for pts having HM after BNTCV to adapt vaccine strategy including boosts or EVUSHELD. The usage of telemedicine connecting system may help to follow the early tolerance and to improve the pts' adherence.

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## ONCOLOGY

### PP15

#### IMMUNOPHENOTYPIC FEATURES OF MOLECULAR SUBTYPES OF BREAST CANCER

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**Introduction:** Currently, immunotropic drugs are used in the modern strategy of cancer treatment. Importance is given to immunological markers of the tumor, which may be associated with the prognosis of the disease, the effectiveness of treatment. Therefore, the study of tumor immunophenotype is one of the leading scientific directions. Of particular interest is the study of the immunophenotypic characteristics of breast cancer depending on its biological subtype. **Purpose:** to evaluate the frequency of expression of HLA-I, HLA-II, CD71, MUC1,0 Pgp170 molecules by breast cancer cells and determine their relationship with the molecular biological subtype of the tumor. **Materials and methods:** This study included 120 patients with breast cancer who received treatment at the Federal State Budgetary Institution "N.N. Blokhin" Ministry of Health of the Russian Federation. Tumor stages II and III prevailed: 56.7% and 33.4%, respectively. A moderate degree of differentiation (G2) was more often noted. The luminal subtype was 58.3% (n=70), non-luminal - in 41.7% (n=50). Immunophenotyping of the primary tumor was performed by immunofluorescence on cryostat sections. The reaction was evaluated using a ZEISS luminescent microscope (AXIOSKOP; Germany). The frequency of expression of HLA-I and class II molecules was studied depending on the clinical and morphological characteristics of breast cancer. The frequency of expression of HLA-I, HLA-II, CD71, MUC1.0 Pgp170 molecules depending on the molecular subtype of breast cancer was studied. **Results:** The absence of molecules of the major histocompatibility complex of class I and II on breast cancer cells was found in 89.6% of the samples. In 23.4% of cases, their monomorphic expression was observed. In the luminal subtype, HLA-II class molecules were expressed somewhat more often: in total, mosaic and monomorphic types of reactions were observed in 30.5% (20/65) of cases. With non-luminal - 20.0% (10/47) of cases. The frequency of expression of the transferrin receptor is significantly higher in the luminal subtype than in the nonluminal subtype: 85.9% (n=5) and 65.2% (n=30),  $p = 0.011$ . Luminal breast cancer cells express transferrin receptors predominantly

monomorphically: 75.4% (n=49) versus 43.5% (n=20) in the non-luminal subtype,  $p=0.003$ . The percentage of monomorphically expressing MUC1 tumors is higher in luminal cancer: 83.3% (n=35) versus 65% (n=26) in the non-luminal subtype. Expression of Pgp70, namely monomorphic, is more often observed in luminal breast cancer. **Conclusion:** Luminal breast cancer is characterized by unfavorable prognostic immunophenotypic features. In the luminal subtype, expression of CD71 is more often observed, predominantly monomorphic. In the non-luminal subtype, expression of Pgp 170 is observed less frequently. No statistically significant differences between the molecular subtypes in terms of the level of expression of HLA-I and class II molecules were found.

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## CHRONIC LEUKEMIAS

PP16

### INFECTIOUS COMPLICATIONS IN CHRONIC LYMPHOCYTIC LEUKEMIA – CHALLENGING ISSUES OF HEMATO-ONCOLOGY

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**Objective:** The aim of the study was to identify the diagnosis features and origin of the infectious complications in chronic lymphocytic leukemia (CLL). **Methodology:** Our observational study enrolled 82 patients (pts) with different CLL phases, who were managed at the Institute of Oncology of Moldova from 2000 to 2022. The pts age ranged between 45-86 years (median age 66.2 years). There were 47 (57.3%) males and 35 (42.7%) females. The diagnosis was proved by histopathological, immunohistochemical, cytological and immunophenotyping examinations. We used IWCLL criteria on a basis of lymphoid cells rate in the blood count and bone marrow aspirate. **Results:** According to Binet classification, stage A was revealed in 54 (65.9%) pts, stage B – in 28 (34.1%). Infectious complications developed in 36 (43.9%) cases. Respiratory bacterial infections were diagnosed in 29 (80.6%) pts, commonly comprised the relapses of chronic bronchitis - in 11 (30.6%) and acute pneumonia - in 10 (27.8%). Herpetic infection was diagnosed in 2 (5.6%) cases. Other infectious complications included nephro-urinary tract in 3 (8.2%) pts and acute otitis in 2 (5.6%). Fatal outcomes occurred in 16 (19.5%) pts, including 6 (37.5%) with infections, 5 (31.3%) with CLL progression. **Conclusion:** The infectious complications proved to be the common manifestations and causes of death in CLL, especially in stage B.

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## PEDIATRIC HEMATOLOGY ABSTRACT CATEGORIES

### COAGULATION AND FIBRINOLYSIS DISORDERS

OP 17

#### THE EFFECT OF THE COVID-19 PANDEMIC PROCESS ON TREATMENT COMPLIANCE IN HEMOPHILIA PATIENTS

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**Objective:** It is known that there were transportation problems to the hospital and treatment experienced in many disease groups during the pandemic process. The negative impact of the pandemic is particularly evident in chronic diseases and in situations that require continuous treatment. In this study, data on access to treatment and disease status in patients with bleeding diathesis were collected by questionnaire method, and the effects of the pandemic on these patients were determined. **Methodology:** Fifty patients who were followed up in Istanbul Medical Faculty Pediatric Hematology-Oncology Department between 2010-2022 with the diagnosis of bleeding diathesis and accepted to participate in the survey were included in the study. Questions were answered by telephone. Responses were analyzed using SPSS. **Results:** The mean age of the patients in our study was 13 years, the age range was between 2-26 years. The median age was 13. Of these patients, 44 (88%) were male and 6 (12%) were female. 88% of the patients were diagnosed with Hemophilia A, 12% with Hemophilia B. While 56% of the patients were receiving prophylaxis for the treatment of hemophilia, 44% were receiving treatment in case of bleeding. Sixtyfour percent of the patients went to a health institution or doctor once every 1-3 months, 18% every 6 months, 6% once a year for control and follow-up purposes. The last drug or dose change was made 0-6 months ago in 16% of the patients, 7-12 months ago in 4%, and 22% 1-2 years ago. However, in 6%, more than 2 years had passed since the last change, and 42% did not change. Serious psychiatric problems were observed in our two patients. Fear of death and anxiety disorder has been seen in a 10-year-old patient. During this period, severe hyperactivity developed in 1 patient. While 10% of the patients interrupted their treatment in the last 3-4 months, 90% did not. The reason for the disruption of the patients who interrupt their treatment is Covid infection in 20% and the drug cannot be obtained in 40%. While 94% of the patients had no problem in the supply of the drug due to the Covid-19 pandemic, 6% had a problem in the supply of the drug. While 33% of the patients who had problems in the supply of the drug received support from their doctor, 33% from the patient association to solve the problem, 33% did not receive any support from anyone. Among the reasons for having problems in

the administration of the drug, 33% of the patients did not go to the hospital because they were afraid of the pandemic, 33% of them could not get treatment even though they went to the hospital, and 33% of them other reasons were reported. While 48% of the patients want an experienced health personnel to go to their home to perform their treatment, 52% do not want it, stating that they do not need it. None of the patients whose treatment was interrupted did not complain of bleeding during this period. **Conclusion:** It was seen that the patients experienced disruptions related to access to medication and treatment during the pandemic process. However, there were no major problems in this process, thanks to the help of their physicians and other institutions. It is important to emphasize the importance of treatment in hemophilia patients and to have easy communication with the center followed in order to overcome the pandemic process without complications.

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## LEUKEMIA

### OP 18

#### EVALUATION OF MRD-STATUS IN POST-INDUCTION PERIOD IN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA.

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**Objective:** The need to study the significance of minimal residual disease (MRD) at the induction therapy in patients with acute lymphoblastic leukemia (ALL) is beyond doubt. This has been confirmed by many years of work by many research groups. The role of MRD in the late stages of treatment and the impact of these values on patients survival requires research and discussion. **Aim:** To evaluate the influence of MRD-status in post-induction period on survival in patients with acute lymphoblastic leukemia. **Methodology:** From 2010 to 2022, 135 patients with primary B-ALL enrolled in ALL-IC BFM 2009 protocol. Median age was 5.4 year (range 1-17). Male was 62 (49,5%) and female 73 (54,1%). The diagnosis was based on WHO 2016 criteria. Stratification on prognostic risk groups was carried out according to protocol criteria. Prednisone response evaluated at day 8 of treatment. The 15th, 33th, and 78th (as post-induction) day response was assessed by bone marrow cytology and level of MRD by flow cytometry. **Results:** 5y-overall survival (OS) for patients with MRD-negative status on day 15 was 94,4±5,4% and 87,0±3,4% for MRD-positive (p=0,5). On day 33 patients with MRD-negative status achieved 5y-OS in 86,7±5,8% and 89,6±3,5% for MRD-positive (p=0,6). 5y-OS for patients with MRD-negative status on day 78 was 90.8±4.0%, MRD-positive - 90,4±6.5%. DFS for MRD-negative status was 88.5±4.5%, for MRD-positive - 66.3±11.8% (p=0,1). EFS for MRD-negative patients was 87.2±4,6% and for MRD-positive 66.3±11.8% (p=0,09). **Conclusion:**

We have found a tendency between MRD status on day 78 and the frequency of relapses in patients. At the moment, there are no reliable data on the effect of post-induction MRD status on survival. The assessment of MRD in the post-induction period has prognostic prospects and requires further study.

<https://doi.org/10.1016/j.htct.2022.09.1225>

## INHERITED BONE MARROW FAILURE DISEASES

### OP 19

#### GHOSAL HEMATODIAPHYSEAL DYSPLASIA (GHDD) DIAGNOSIS AND TREATMENT: CASE REPORT

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**Objective:** Ghosal hematodiaphyseal dysplasia syndrome (GHDD) is a rare autosomal recessive disorder characterized by increased bone density and regenerative corticosteroid-sensitive anemia. We describe GHDD in an 11-year old Azerbaijani boy with refractory anemia, mild thrombocytopenia and radiological metadiaphyseal dysplasia. The diagnosis was made based on clinical and laboratory examinations and genetic analysis. We have observed a significant improvement of anemia after administration of steroids. **Case report:** An 11-year-old boy with long-standing anemia, complained of fatigue, delayed physical development, and limited range of motion in the joint. Physical examination did not reveal LAP and hepatosplenomegaly. Among the dysmorphic craniofacial changes mentioned in the literature, has a tower-shaped skull, micrognathia, drooping ears, a long and wide philtrum, and a thin upper lip. Skeletal X-ray imaging showed fibrotic changes and varying degrees of osteopenia in the metaphysis of the long tubular bones. **Methodology:** The blood count: Hb 7.0 g/dL, HCT 24.5%, reticulocytes 5.6%, MCV 78 fL, MCHC 28.6 g/dL, WBC count 6860/mm<sup>3</sup>, platelets 165000/mm<sup>3</sup>, ESR 75 mm/h, anisocytosis in erythrocytes and platelets were observed in a peripheral blood smear. Hemoglobin electrophoresis, iron studies, vitamin B12 and folic acid were normal. Coombs test was negative. Bone marrow examination showed hypoplasia in erythroid and megakaryocytic series and dysgranulocytopenia. **Results:** After detection of exon 12 (p. Gly473Trp), rs149988492, CM215867) in the genetic panel analysis of anemia, steroid treatment at a dose of 1 mg/kg/day was started and anemia improved at 1-month follow-up (Hb level 6.8 g/dL to 11.9 g/dL), but mild thrombocytopenia was noted to persist. The clinically insignificant CRP elevation normalized during the treatment. **Conclusion:** GHDD should be



considered in patients with clinical and radiographic evidence of diaphyseal dysplasia as well as hematological abnormalities. In addition, bone dysplasia should be investigated in treatment-resistant hematological pathologies of unknown origin. Although GHDD is rare, clinicians should be informed that it responds well to steroid therapy.

<https://doi.org/10.1016/j.htct.2022.09.1226>

#### HEMOGLOBINOPATHIES (SICKLE CELL DISEASE, THALASSEMIA ETC...)

OP 20

##### COMPARISON OF THE QUALITY OF LIFE OF PATIENTS WITH A BETA-THALASSEMIA MAJOR, REGULARLY RECEIVING PARENTERAL AND ORAL CHELATORS

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**Objective:** Patients with  $\beta$ -thalassemia major ( $M\beta$ -th) are transfusion-dependent, which affects their quality of life. To maintain a safe level of iron in the body, patients with  $M\beta$ -th require adequate regular therapy with chelation drugs (CP). Currently, for the correction of iron overload in patients with  $M\beta$ -th, along with oral CP, parenteral CP continues to be used. However, oral and parenteral CP are perceived by patients ambiguously. Comparative assessment of the quality of life of transfusion-dependent children with  $M\beta$ -th receiving various CPs: parenteral deferoxamine and oral deferasirox. **Methodology:** For 2 years, a survey and clinical observation of 201 children with  $M\beta$ -th aged 2 to 18 years (boys 128, girls 73) was conducted. The control group consisted of apparently healthy children from preschool and school institutions ( $n=30$ ). Patients with  $M\beta$ -th underwent a quality of life study (PedsQL- Pediatrics Quality of Life Inventory, Generic Core Scales and PedsQLTM4.0) and a psychological examination. The survey was conducted after obtaining the informed consent of the parents of older children at the beginning and at the end of the study. Once a month, the necessary clinical and biochemical analyzes were carried out. Patients with  $M\beta$ -th regularly prescribed various CP regimens: deferoxamine subcutaneously; deferasirox, orally. **Results:** All studied patients with  $M\beta$ -th were divided into four age groups: group 1 - children under 4 years old according to parents ( $n=41$ ); group 2 - children 5-7 years old according to the assessment of children and parents separately ( $n=62$ ); group 3 - children 8-12 years old according to the assessment of children and parents separately ( $n=47$ ); Group 4 - children aged 13-18 years old according to the assessment of children and parents separately ( $n=51$ ). Each of the 4 groups of  $M\beta$ -th patients was divided into a subgroup taking only deferiprone and a subgroup taking only deferasirox. **Conclusion:** According to the Results of the survey, the indicators of the quality of life and the psychological state of children with  $M\beta$ -th receiving

parenteral and oral CP differed. So, in sick children with  $M\beta$ -th of different age groups, when taking parenteral CP in comparison with those taking oral CP, the quality of life was reduced, and the psychological state worsened significantly. This was especially impacted patients in the group of 8-13 years. In this group, there were more complex relationships with peers, parents, there was an increase in anxiety and aggressiveness, which is associated with the need for hours of use of the pump for subcutaneous injection of the drug, the presence of pathology that limits the use of oral chelators. In children of 4 different age groups, there is a significant difference in the values given by patients and their parents to the quality of life in patients receiving parenteral and enteral chelator therapy.

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#### LYMPHOMAS

OP 21

##### LABORATORY AND CLINICAL FEATURES OF TUMOR LYSIS SYNDROME IN CHILDREN WITH HIGH-GRADE NON-HODGKIN LYMPHOMA AND EVALUATION LONG-TERM RENAL FUNCTIONS IN SURVIVORS

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**Objective:** Tumor lysis syndrome (TLS) describes biochemical and clinical abnormalities resulting from spontaneous or treatment-induced necrosis of rapidly proliferating tumors such as Burkitt's lymphoma (BL). TLS can lead to complications like acute kidney injury (AKI) which can be fatal. In patients who had AKI in childhood, the frequency of kidney problems increases in later ages. Therefore, there is a need to examine long term kidney functions in patients with TLS. The purpose of our study is to investigate the laboratory and clinical features of tumor lysis syndrome in childhood non-Hodgkin lymphomas (NHL) and to reveal its impact on long term kidney function in survivors. **Methodology:** Our study was a single center retrospective study. 107 patients (0-18 years of age) admitted to our hospital between 1998-2020 years with a diagnosis of NHL and who received chemotherapy were included in the study. Clinical and laboratory characteristics of the patients at the time of diagnosis and within 14 days from the start of chemotherapy were examined. The presence of TLS and its laboratory and clinical features were examined according to the Cairo-Bishop criteria. The relationship between TLS and age, gender, histopathological subgroup, tumor stage, lactate dehydrogenase (LDH) level at presentation, bone marrow and kidney involvement were investigated. The presence of AKI was determined according to the Kidney Disease: Improving Global outcomes criteria.

Long-term renal functions of the patients were investigated. **Results:** 80.3% of the patients with a median age of 9.8 years were male. The most common histopathological subgroup was BL (77.5%), while the majority of patients (76.7%) had advanced disease. Clinical TLS (CTLS) was observed in 12.1% of the cases, and isolated laboratory TLS (LTLS) was observed in 18.7%. Hyperhydration±alkalinization and allopurinol were used in first-line treatment and prophylaxis. A significant correlation was found between young age, advanced stage, high lactate dehydrogenase level at presentation and LTLS. Bone marrow involvement was found to be significantly higher in the group with CTLS. AKI was observed in 12.1% of the patients. Out of a total of 103 patients whose treatment was completed, 93 (90.3%) patients survived and 10 deaths were observed. No death due to TLS was observed. The mean survival time was  $215.55 \pm 7.502$  months. After an average of 6.9 years, when the glomerular filtration rate values of the patients at the first admission and at the last admission were compared, a mean decrease of 10 mL/min/1.73 m<sup>2</sup> was detected. However, it was not found to be statistically significant. **Conclusion:** In our study, lower age, advanced stage, high LDH level at presentation were found to be risk factors for TLS. Long-term renal function loss was not detected in the survivors, for whom early and careful prophylaxis/treatment approaches were applied for TLS. The survivors are still being followed up.

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#### SUPPORTIVE CARE AND PALLIATIVE CARE

##### OP 22

#### IMPACT OF COVID-19 PANDEMIC ON DELAY OF CHILDHOOD CANCER DIAGNOSIS AND THE OUTCOMES IN A PEDIATRIC HEMATOLOGY/ONCOLOGY DEPARTMENT

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Aslınur OZKAYA PARLAKAY<sup>1</sup>,  
İnci ERGURHAN ILHAN<sup>1</sup>

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**Objective:** Restriction of access to healthcare during COVID-19 pandemic is undoubtedly a major problem for patients with cancer. Although childhood cancers are highly curable, it is obvious that diagnostic and treatment disruptions will lead to poor Results. In this study we investigated the effects of pandemic on diagnosis and treatment delays of children with cancer along with their consequences. **Methodology:** We searched all pediatric patients treated for cancer between March 2020 and January 2022 for COVID-19 infection. Data were collected collected from medical files of patients diagnosed with COVID-19, confirmed by polymerase chain reaction (PCR), who received active antineoplastic treatment. **Results:** Fifty-eight patients developed COVID-19 infection at

different stages of their anticancer treatment. Twenty-five had an asymptomatic COVID-19 infection, twenty-six had mild symptoms, three had moderate symptoms and four had severe disease. All of them recovered from COVID-19 infection. Chemotherapy courses were continued during active infection in four patients and interrupted in other patients. **Conclusion:** While strict measures are required to control the pandemic, patients with severe critical illness such as cancer should be carefully evaluated and treatment delays that may have vital consequences should be avoided. In pediatric patients with cancer whom infected by COVID-19, continuation of anticancer treatment may be considered by evaluating the clinical status of the patient.

<https://doi.org/10.1016/j.htct.2022.09.1229>

#### TUMOR BIOLOGY, IMMUNOLOGY AND IMMUNOTHERAPY

##### OP 23

#### INTRAPLEURAL THERAPY TO DISRUPT IL-6/IL-8 JUXTACTINE SIGNALLING TO BLOCK TUMOR EMT AND TO DRIVE SYSTEMIC ANTI-TUMOR IMMUNITY

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<sup>2</sup> AHN

**Objective:** The goal of this study was to determine whether antiIL-6R $\alpha$  block (tocilizumab) will alter the pleural secretome and will diminish tumor-specific immune responses. **Methodology:** Pleural T cells were isolated from freshly drained pleural effusions (n=6). Autologous pleural tumor was expanded in vitro using the Mammary Epithelial Growth Medium (Lonza). Pleural T cells were stimulated using anti-CD3/CD28 Dynal beads and low dose IL-2 (60 Cetus U/ml) for 2,4,7, 14 or 21 days in the presence of tocilizumab for the last 48h (0, 0.35, 0.72, 1.43, 2.86 and 5.72ug/ml). Pleural T cell effectors were counted and plated on tumor targets at 12.5:1 E:T in the presence of tocilizumab. **Results:** Ex vivo expanded pleural T cells were effector-memory phenotype (CD45RA-CD27-) and were highly cytotoxic against autologous tumor (89-100%). The majority of CD8+ T cells were central memory (CD45RA-/CD27-) or effector memory (CD45RA+/CD27-); the majority co-expressed granzyme B, perforin, 20-60% expressed PD-1. Most CD4+ co-expressed granzyme B and perforin and were PD-1+, suggesting cytotoxic CD4+ T cells. The presence of tocilizumab reversed tumor EMT but did not alter cytotoxicity. **Conclusion:** We show that the IL-6/IL-6R $\alpha$  axis is prominent in MPE, drives tumor growth and inhibits anti-tumor immunity. Pleural T cells are neither exhausted nor dysfunctional but are suppressed by the pleural environment. Ex vivo expanded MPE CD8 and CD4 T cells are highly cytotoxic against

autologous tumor. Anti-IL-6R $\alpha$  block reverses tumor EMT but does not inhibit effector responses.

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#### OP 24

##### NIVOLUMAB EXPERIENCE IN PEDIATRIC MALIGNITIES

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**Objective:** Nivolumab is a human monoclonal antibody to programmed cell death receptor 1 (PD-1) that acts as an immune checkpoint inhibitor and is used in the immunotherapy of various types of advanced or metastatic cancer. The aim of this study is to evaluate the efficacy of nivolumab in pediatric patients with various highly malignant tumors and to share the experience of Ankara University Pediatric Oncology Department. **Methodology:** Eight patients were included in the study. Median age at diagnosis is 11.3 years (min 4.9- max 13.9). Treatment indications were malignant mesothelioma<sup>(1)</sup>, rectal adenocarcinoma<sup>(1)</sup>, malignant melanoma<sup>(1)</sup>, ewing sarcoma<sup>(2)</sup>, osteosarcoma<sup>(1)</sup>, non-hodgkin lymphoma<sup>(1)</sup> and hodgkin lymphoma<sup>(1)</sup>. **Results:** Four patients died due to progressive disease. Complete remission was achieved in four patients diagnosed with malignant mesothelioma, rectal adenocarcinoma, malignant melanoma and Hodgkin lymphoma. **Conclusion:** Immune checkpoint inhibitors are one of the greatest advances in oncological therapy and improve the overall survival of patients with advanced and resistant malignancies. More studies are needed to evaluate the efficacy of immune checkpoint inhibitors in pediatric tumors.

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##### PEDIATRIC LEUKEMIAS

#### OP 25

##### MRD IN BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM

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**Objective:** Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is an extremely rare disease with an aggressive course. Plasmacytoid dendritic cells (PDCs) are a component of the innate immune response: they secrete large amounts of type I interferons. There are several fractions of PDC in normal bone marrow: (CD123+CD4+CD56+) and (CD123+CD4+CD56-). PDC fraction CD123+CD4+CD56+ is a non-tumor analogue in BPDCN. Normally, the ratio of CD56+PDCs to CD56-negative PDCs is 0.129 $\pm$ 0.144. **Methodology:** AIM. Determination of the principles for assessing minimal residual disease (MRD) in the bone marrow by flow cytometry in BPDCN. **Materials and methods:** In the following case, the diagnosis of BPDCN with lesions of the skin, bone marrow, and spleen was established using the IHC study of the skin biopsy, morphological, flow cytometric studies of the bone marrow, as well as CT of the chest and abdomen. In a diagnostic flow cytometric study of the bone marrow, tumor cells expressed CD56, CD4, CD123 **Results:** At the end of the treatment stages, MRD was determined by flow cytometry. Isolation of CD56-positive PDCs was carried out on the basis of light scatter parameters, nucleotropic dye SYTO41, weak expression of CD45, co-expression of CD4, CD56, CD123. In the analysis, the ratio of CD56-positive PDCs to CD56-negative PDCs increases from 0.063 to 8.9, while the number of blasts (1.2%) and the proportion of CD56-positive PDCs among myelokaryocytes (0.06%) changes slightly. One month later, the relative content of CD56-positive cells was 81.2% of the PDCs, while the morphological study showed an increase in the number of blasts to 5.2%. One more month later, blast cells numbered 85% in the bone marrow punctate. **Conclusion:** In the described case, the dynamics of the ratio between CD56-positive and CD56-negative PDCs showed an increase in the tumor clone in the relapse of the disease. The change in this ratio became noticeable in the analysis of hypocellular bone marrow in the absence of an increased number of blasts in the morphological study of this sample. Measurement of the ratio of CD56+CD123+CD4+ cells to CD56-CD123+CD4+ cells is an effective strategy for objective assessment of tumor burden and the likelihood of bone marrow tumor recurrence of blastic plasmacytoid dendritic cell neoplasm.

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#### OP26

##### EVALUATION OF MICROBIOLOGICALLY DOCUMENTED BLOODSTREAM INFECTIONS IN PEDIATRIC HEMATOLOGY/ONCOLOGY PATIENTS: RESULTS OF TEN YEARS

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**Objective:** In pediatric hematology/oncology patients, infections are the main cause of prolonged hospital stay, increased mortality and high cost following relapse or progression. In this patient group, infections caused by multi-drug resistant bacteria are common and affect morbidity and mortality rates. We aimed to determine the frequency and antibiotic susceptibility of bacteria isolated from blood cultures of the patients with malignant and non-malignant diseases in our hospital over a ten-year period. **Methodology:** patients admitted to the Pediatric Hematology/Oncology Service between January 2011- June 2021 were evaluated. The most common disease was acute lymphoblastic leukemia (27%). The first isolated bacteria of same species for each patient were included, contaminated cultures were not included. Blood cultures incubated in the Bactec FX automated blood culture system for five days. Bacteria were identified by conventional methods or automated systems. Antibiotic susceptibility tests were performed by disc diffusion or gradient test and were evaluated according to guidelines. **Results:** A total of 4631 blood culture samples from 296 patients were analyzed. Positive signal was seen in 620 samples. Blood culture positivity was 13.4%. Total 298 blood culture samples were evaluated. Gram positive bacteria rate were 59% and 41% gram negative. The most frequently (58.7%) isolated gram positive bacteria were methicillin-resistant coagulase negative staphylococci and gram negative bacteria were *Klebsiella pneumoniae* (28,5%). The rate of bacteria producing extended spectrum beta lactamase (ESBL) was detected as 74% for *Escherichia coli* and 69% for *Klebsiella pneumoniae*. **Conclusion:** It is important for each center to determine its own causative agents and their resistance patterns in bloodstream infections. Gram positive bacteria were found dominantly in our study. The high ESBL rate in *E.coli* and *K.pneumoniae* isolates is remarkable. Early detection of the causative agents in bloodstream infections of the pediatric hematology/oncology patients and initiation of prompt treatment are important to reduce mortality.

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## NURSING

### PSYCHOLOGICAL SUPPORT FOR CANCER PATIENTS

#### OP 27

#### INFLUENCE OF CANCER NEWS ON QUALITY OF LIFE OF PATIENT'S FAMILIES: AN OBSERVATIONAL STUDY

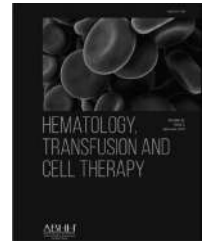
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**Objective:** Malignant disease diagnosis brings great psychological suffering to the patient, and the sickness might have catastrophic ramifications for the relatives. The Objective of this study is to assess influence of cancer news on quality of life of patient's families. **Methodology:** This study was prospective cohort study conducted at the oncology department of a tertiary care Hospital, Pakistan for the duration of one year. The quality of life was assessed as per pre-defined questionnaire both from two first degree relatives at each clinical visit during treatment every week and every month for six months after completion of treatment. Data analysis was done by employing SPSS version 21. **Results:** 180 family members were included. QOL of family members was  $1.54 \pm 0.57$  ( $p=0.001$ ). Anxiety/depression score of the family members was  $1.67 \pm 0.64$  while in control group it was  $1.50 \pm 0.64$  ( $p=0.031$ ). The EQ VAS score in control group was  $66.5 \pm 16.7$  whereas in caregivers group, it was  $71.3 \pm 18.8$  ( $P=0.023$ ). Stress was observed in 98 (54.44%) participants in caregivers group. Moderate-severe depression was observed in 45(25%) vs 21(11.67%) participants in caregivers vs control group, respectively ( $p=0.041$ ) **Conclusion:** Our findings reveal that family caregivers of cancer patients face mental health issues and a decline in health-related quality of life. To reduce the effect of caring on the mental health and health related quality of life of family caregivers in Pakistan, culturally suitable caregiver support programs are required.

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## POSTER PRESENTATIONS

### ADULT HEMATOLOGY ABSTRACT CATEGORIES

#### CHRONIC LEUKEMIA

PP 01

#### MOLECULAR ASPECTS IN CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS WITH AUTOIMMUNE CYTOPENIAS: SINGLE CENTER EXPERIENCE

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Marija Popova Labacevska,  
Aleksandra Pivkova Veljanovska,  
Simona Stojanovska, Dushko Dukovski,  
Milche Cvetanoski, Lazar Cadievski,  
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**Objective:** Autoimmune cytopenia's, particularly autoimmune hemolytic anemia (AIHA) and immune thrombocytopenia (ITP), complicate up to 25% of chronic lymphocytic leukemia (CLL) patients. Their occurrence correlates with a more aggressive disease. AIHA and ITP are more frequently found in patients with unfavorable biological risk factors for CLL. B lymphocytes at CLL are responsible of pathogenic mechanisms, involving aberrant antigen presentation and cytokine production. The aim of this study was evaluation of autoimmune cytopenia's in chronic lymphocytic leukemia patients from Republic of North Macedonia in correlation with genetic structure of pathologic B lymphocyte. **Methodology:** This is a retrospective study of patients with CLL, diagnosed and followed in the period between January 2011 and January 2021. Individual data from 100 treatment naïve CLL patients were analyzed, and mutational status and configuration of IGHV-IGHD-IGHJ rearrangements and genetics were analyzed using reverse transcriptase– polymerase chain reaction (RT-PCR) and sequencing methodology at the center for bimolecular pharmaceutical analyses, faculty of pharmacy, Skopje, Republic of North Macedonia. **Results:** Our 2531-1379/

evaluation have shown that 10% of CLL patients had AIHA and 4% had ITP. Most of the patients with autoimmune cytopenias had unmutated IGHV genes. The most frequently expressed IGHV subgroup was IGHV1-69 (71%), followed by IGHV3-13 and IGHV4-4 (14%). The genetic results presented unfavorable cytogenetics with 11q deletions and NOTCH mutation. **Conclusion:** The results of our study are consistent with published studies with specific molecular signature.

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#### CHRONIC MYELOPROLIFERATIVE DISEASES

PP02

#### FOLLOW-UP OF CHRONIC MYELOID LEUKEMIA PATIENTS WHOSE TYROSINE KINASE TREATMENT WAS STOPPED: CASE SERIES

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**Introduction:** Chronic Myeloid Leukemia (CML) is a myeloproliferative disease characterized by the formation of the BCR ABL1 fusion protein with translocation t(9;22) (Philadelphia chromosome-Ph). With recent studies, it has been understood that the treatment of adult chronic phase CML patients who have achieved a deep molecular response with the use of TKI and can maintain this response for a long time can be safely terminated; It has been observed that it is possible for patients to remain in long-term molecular remission without the use of TKI. Based on these studies, we will try to present the follow-up processes of chronic phase CML patients, who were followed up in our clinic and whose TKI treatment was stopped. **Case reports:** First case; A 69-year-old female patient was diagnosed with Ph positive chronic phase CML in 2008. The imatinib treatment of the patient, who had been using imatinib for about 13 years and was bcr-abl negative for the

last 3 years, was discontinued in December 2021. In the 2nd and 4th months, the requested bcr-abl was negative. Second case; a 42-year-old male patient was diagnosed with Ph-positive chronic phase CML in 2006. The patient, who had been using imatinib for about 16 years and was bcr-abl negative for the last 3 years, was discontinued in April 2022. bcr-abl came back negative. Third case; a 42-year-old female patient was diagnosed with Ph positive (IS: 31,824) chronic phase CML in 2019. He received Nilotinib and Dasatinib treatment after he had an allergic skin reaction using imatinib for about 2 years. The patient had drug intolerance and was bcr-abl negative for about 2 years, and the treatment was stopped. The 1-month follow-up was negative for bcr-abl. Fourth case; Imatinib was started in a 50-year-old female patient with the diagnosis of Ph-positive chronic phase CML in 2012. Due to imatinib intolerance, the treatment of the patient who was using nilotinib and was bcr-abl negative for the last 3 years was discontinued in February 2021. The bcr-abl negativity continues in the follow-ups. Fifth case: A 58-year-old female patient was diagnosed with Ph-positive chronic phase CML in 2013. The imatinib treatment of the patient, who has been using imatinib for about 8 years and has been negative for bcr-abl for the last 3 years, was discontinued in November 2021. The bcr-abl negativity continues in the follow-ups. **Conclusion:** STIM 1 (Stop Imatinib) study is the first multicenter, non-randomised, prospective study on TKI termination. Then, TWISTER, A-STIM, ENEST, STOP2GTKI, EURO SKI studies were carried out. In these studies, TKI treatment was discontinued in patients who used TKI for at least 3 years and had a major molecular response for the last 2 years. Remission was achieved in approximately 50% of the patients who were followed up without medication. In our study; The treatment of patients who had been using TKI for 5 years and had a major molecular response for about 2 years was stopped. The follow-up of the patients (minimum: 1 month, maximum: 15 months) continues, and all of them are in remission.

<https://doi.org/10.1016/j.htct.2022.09.1237>

#### PP 03

##### TREATMENT-FREE REMISSION IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA: MANAGEMENT APPROACHES

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**Objective:** The study objective was to analyze the short- and long-term results of treatment discontinuation in patients with chronic myeloid leukemia (CML) and complete molecular response (CMR). **Methodology:** This prospective study enrolled 22 patients (pts) with chronic phase of CML, managed at the Oncologic Institute from Moldova between 2017–2022. The age range was 29–73 years. The male/female ratio was 1:1.2. The real-time quantitative PCR revealed the wide range of BCR-ABL p210 transcript: 21.84–100% IS. In 7 (31.8%) pts the rate of BCR-ABL p210-positive cells was less than 50%.

CMR was achieved in 15 (68.2%) pts after imatinib therapy and in 7 (31.8%) pts after the 2nd generation of TKIs. **Results:** The therapy with TKIs was stopped due to the different reasons in all patients after the CMR was obtained. Two (9.1%) pts stopped the TKIs treatment due to the pregnancy. The molecular relapse occurred in 6 (27.3%) pts, including one pregnant female. All relapsed pts had the initial BCR-ABL p210 transcript expression > 50%. The CMR span ranged between 2.5–26 months in relapsed pts. The range of BCR-ABL p210 transcript in the relapsed pts was 0.002–0.56%. These pts achieved the 2nd CMR after restarting TKIs treatment. All pts are alive, with the ECOG score of 0–1. **Conclusion:** TKIs discontinuation may be considered an option in CML patients with CMR, especially in those with the initially low BCR-ABL p210 transcript expression. The 2nd CMR may be obtained after restarting the TKIs treatment in pts with minor molecular relapse.

<https://doi.org/10.1016/j.htct.2022.09.1238>

#### COAGULATION DISEASES

##### PP 04

##### PHENOTYPE/ GENOTYPE SCREENING PATTERN OF HEMOPHILIA A AND B IN SAUDI ARAB

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**Objective:** Hemophilia A and B are X-linked recessive bleeding disorder caused by variants in the factor VIII (FVIII) and factor IX (FIX) genes. There is correlation between the type of mutation and clinical severity of these patients. Establishing national screening program for haemophilia patients is highly encouraged by the World Health Organization (WHO) and World Federation of Haemophilia (WFH). Hence we aimed to establish a genotypic data base for the nature of mutations present in Saudi population. **Case report:** This retrospective descriptive study on a cohort of 136 Saudi hemophilia A and B patients. **Methodology:** Molecular studies were performed to identify known and novel causative variants in hemophilia A and B families and correlated with some clinical features. **Results:** There were 129 male and 7 females with age ranged from 2 - 62 years old, 97 (71.3%) hemophilia A (HA) and 39

(28.7%) hemophilia B (HB). The clinical severity of hemophilia A ranged between mild (10, 10.3%), moderate (2, 2.1%) and severe (83, 85.6%), while for hemophilia B (mild 13 (33.3%), moderate 2 (5.1%) and severe 24 (61.5%) respectively. There were 76 (55.9%) had chronic joint disability. Factor inhibitors with different titers were detected in 24 (24.7%) of HA and only 2 (5.1%) of HB. Out of the whole cohort 136 had been tested for causative variants, 17 (12.5%) were positive for inv-22 and 4 (2.9%) for inv-1, while all negative HA were selected for analysis by next generation sequencing. We are reporting 3 cases of females with severe forms of hemophilia. We are reporting different mutations that was consistent in group of tested members of same family/trip. We confirmed as previously reported high frequency of inv 22 and we found 7 novel mutation out of 12 detected variants for HA and one novel mutation out of 13 detected variants for HB. **Conclusion:** These results will enrich the spectrum of variants and enlarge the factor VIII and factor IX proteins database in the Saudi Arabian population. Establishing a molecular genetic based tests for fast, easy, and cost effective reliable mutation screening that can also be applied in the future for prenatal and pre-implantation genetic diagnosis.

<https://doi.org/10.1016/j.htct.2022.09.1239>

#### PP05

##### SERUM LEVEL OF VASCULAR CELL ADHESION MOLECULE AND P SELECTIN AS THROMBOPHILIC RISK FACTOR FOR EARLY VASCULAR ACCESS THROMBOTIC OCCLUSION IN HEMODIALYSIS PATIENTS

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**Objective:** Hemodialysis (HD) vascular access (VA) failure is the dominant cause of morbidity and the major cost of care for ESRD patients. The aim of the present work is to assess the serum level of vascular cell adhesion molecule and P-selectin in HD patients as markers for early thrombotic VA event. **Methodology:** 90 CKD patients divided into three groups: group I: 10 subjects apparently health, group II: 10 Patients with CKD stage IV-V on medical treatment and group III: 70 Patients with CKD stage V on HD with recent VA insertion divided into 2 subgroups: Subgroup III a: 57 patients with AV shunt and subgroup III b: 13 patients with permanent catheter. Laboratory investigations done (blood urea, serum creatinine, eGFR, CBC, PT, and INR), imaging and serum VCAM 1, P selectin before and 6 months after HD **Results:** There was positive connection between VCAM and P selectin and dialysis with statistics in form of p value (<0.001). Markers level pre dialysis and after 6 months of dialysis revealed that range of p selectin and VCAM1 level after 6 months are higher than pre dialysis level. **Conclusion:** Detection of elevated serum level of circulating sVCAM-1 and s P-selectin could be useful in the prediction of native AVF and

permanent catheter thrombosis in chronic HD patients. The association between sVCAM-1 and s P-selectin and thrombosis in HD patients increases the evidence of the role of adhesion molecules in VA thrombosis

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#### PP06

##### SUCCESSFUL MANAGEMENT OF SEVERE CONGENITAL FACTOR X DEFICIENCY DURING PREGNANCY AND LABOR WITH PCC IN TWO SISTERS

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**Introduction:** Factor X (FX) deficiency is an autosomal recessive disorder caused by quantitative or qualitative defects in the FX protein. FX deficiency has an estimated worldwide prevalence of one in 1000000. <sup>(1)</sup> Pregnancy in women with congenital FX deficiency has been associated with adverse fetal outcomes (abortion and preterm labor) (2,11). We report two cases of successful pregnancy with factor X deficiency. **Case 1:** A 29-year-old woman with congenital factor X deficiency and prior abortion on prophylaxis PCC every 4 weeks. She was treated with PCC 25unit/kg twice weekly during the pregnancy course. At week 32 of pregnancy, she presented with labor pain. Lab showed PT 20.7 PTT 52.5 INR1.5 Fibrinogen 3.8 Hb13.8 platelet 195 WBCs 7.6 factor X 0.15. She was given PCC 25 units/kg until a level of 0.4 was achieved. She delivered a healthy, 1.9 kg baby by normal vaginal delivery. The estimated blood loss was 150 ml. She then received FX 15 units/kg for 3 days postpartum to maintain FX level >30% and INR <1.5. No episodes of abnormal bleeding were observed during pregnancy, labor or postpartum. **Case 2:** A 36-years-old woman with congenital factor X deficiency and two prior abortions, on prophylaxis PCC every 4 weeks. She received prophylaxis PCC 25units/kg twice weekly during the course of this pregnancy. At week 38 of pregnancy, she delivered a healthy 3.2 kg baby by cesarean section (CS) after failing labor induction. Lab showed PT 23.7 PTT 50.4 INR1.7 Fibrinogen 2.3 CBC was normal.FX 0.13. She was given PCC 25 units/kg until a level of 0.4 was achieved. The estimated blood loss was 500 ml. She then received FX 15 units/kg for 7 days postpartum to maintain FX level >30% and INR <1.5. She was discharged on tranexamixc acid. No episodes of abnormal bleeding were observed during pregnancy CS or post-partum. **Discussion:** Although FX activity increases during normal pregnancy, levels usually remain insufficient for hemostasis at delivery in women with severe FXD (4,5,6). FX replacement therapy with PCC or FX concentrate may be required to treat or prevent bleeding in FXD. Therefore, a therapeutic dose of PCC 20–30 iu/kg is expected to increase plasma FX activity by 0.4–0.6 iu/ml. Further infusions at 1- to 2-d intervals may be required if sustained treatment is necessary <sup>(3)</sup>. There are reports of FX replacement with PCC during pregnancy in women with previous adverse pregnancy outcomes (7,8) and FX

replacement during labor with PCC or FFP, but with different regimens<sup>(9)</sup>. Our patients were treated with PCC prophylaxis during pregnancy and 25 units/kg during labor. No bleeding nor thrombosis was seen in both cases. The British guidelines recommend PCC 20–40 iu/kg during the third trimester for women with history of bleeding and with FX activity <03 iu/ml with the goal of achieving FX activity >04 iu/ml. They also recommend, to consider further PCC 10–20 iu/kg once daily to maintain FX activity >03 iu/ml for at least 3 days post-partum.<sup>(10)</sup> **Conclusion:** Prophylactic PCC resulted in excellent hemostasis in two of our patients, including one that delivered by C-section.

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## LYMPHOMA

### PP 07

#### PREVENTION CAN BE THE BEST TOOL FOR ADULT T-CELL LEUKEMIA. UPDATED T-CELL BRAZIL PROJECT

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**Objective:** T-cell Brazil project started in April 2017 an ambispective study focusing to collecting epidemiological and clinical data from the most frequent subtypes of PTCL, among them the ATL. As of July 2022 T-cell Brazil database contained 81 (16%) ATL out of 520 registered cases. Our goals are to describe demographic and clinical features, analyze the overall and progression-free survival (OS and PFS), and try to identify factors that could influence outcome. **Methodology:** Brazilian Registry using REDcap Platform by Vanderbilt realized descriptive and bivariate analyses, then it was applied Kaplan-Meier method and log-rank test to obtain survival

estimates, and besides that, it was used the Cox Regression to identify any factor that could influence the OS and PFS. **Results:** The median age was 52 years (24-91); 32 (39%) male; the majority of clinical subtypes were 52% lymphoma type; 81% received chemotherapy. The best response assessment after first-line treatment was: progression or no response in 31%; 26% complete response; 21% partial response, 21% not available (NA) due to death or on treatment; 34% of patients were alive and the 24-month OS and PFS was 33% and 21%, respectively. As predictors for PFS and OS were B symptom and elevated LDH values. **Conclusion:** This study, even recognizing a limited sample size, highlights the poor prognosis associated with ATL, mainly acute and lymphoma type, with high mortality rates. Hence, apparently, a good shot, it would be one of the bases for the prevention of ATL to establish a disease entity of “chronic active HTLV-1 infection” that defines high-risk carriers for ATL development, and then, enables preventive intervention.

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### PP08

#### AN UNUSUAL OCULAR LYMPHOMA, PRIMARY INTRAVITREAL LYMPHOMA DIAGNOSED INCIDENTALLY

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**Objective:** Ocular lymphoma involvement can be either secondary during systemic lymphoma or primary. Diagnosis can be troublesome due to insidious disease onset. Uveitis is the main differential diagnosis. The prognosis is poor. **Case report:** A 62-year-old male patient was evaluated during a periodical check-up for hypertensive retinopathy. The unexpected good vision quality with severe left vitreous infiltration and not associated macular edema contributed to malignancy suspicion. A diagnostic procedure was performed bilaterally. Both of the vitreal tissue revealed atypical lymphoid cells with B-Cell phenotype. Cranial MRI, PET-CT, and CSF analysis documented the case as primary vitreoretinal lymphoma (VRL). **Methodology:** First-line treatment was with intravitreal methotrexate (MTX). After 10 courses, high-dose cytarabine-based treatment was given as consolidation. Considering high recurrence rates, stem cells were mobilized and cryopreserved for future use for autologous stem cell transplantation (ASCT). **Results:** Follow-up was 3 monthly. After 10 months of remission period, retinal disease relapse was spotted. After 5 cycles bilateral intravitreal



MTX, disease progressed as leukemic invasion of left optic nerve. High dose chemotherapy followed by ASCT was performed. **Conclusion:** Diagnosis of IVL is challenging due to late onset macular edema. Related with high relapse rates with high mortality, high-dose chemotherapy is the recommended management type currently.

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PP09

#### THE RELATIONSHIP BETWEEN FERRITIN LEVEL AND THROMBOSIS IN PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA

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**Objective:** Cancer is a well-known condition associated with its treatment and follow-up and increases the risk of thrombosis. As with solid tumors, the risk of venous thromboembolism (VTE) is quite high in lymphomas, especially high-grade B-cell lymphomas. Diffuse large B-cell lymphoma (DLBCL) patients are the most important part of this group. The aim of our study is to determine the effect of ferritin level at the time of diagnosis on thrombosis in DLBCL patients. **Methodology:** In this retrospective study, 133 patients who applied to SBU Dışkapı Yıldırım Beyazıt Training and Research Hospital Hematology clinic and were diagnosed with DLBCL were included in this retrospective study. Demographic characteristics, disease-related findings, presence of central venous catheter and laboratory results of the patients were recorded. **Results:** The median age of the patients included in the study was 63.13±14.85 years. There were 67 female and 66 male patients, stage 1-2: 54 patients, stage 3-4: 79 patients at the time of diagnosis. Thrombosis was observed in 16 of the patients. Median ferritin levels were 357.42 ug/L and 253.07 ug/L, respectively, between the group with and without thrombosis (p:0.026). The ferritin value, which was examined for the presence of thrombosis, was determined as 227 ug/L as a result of the ROC analysis. In the logistic regression analysis, the risk of developing thrombosis was 6.1 times higher in those with a ferritin level ≥227 ug/L. **Conclusion:** Hyperferritinemia may be an independent risk factor for the development of thrombosis in DLBCL patients. In case of hyperferritinemia in patients, initiation of thromboprophylaxis may be an appropriate approach.

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PP 10

#### RITUXIMAB INDUCED LUNG DISEASE IN A MANTLE CELL LYMPHOMA PATIENT RECEIVING MAINTENANCE: CASE PRESENTATION

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**Introduction:** Rituximab-induced lung disease (R-ILD) is a rare entity that should be considered in patients treated with rituximab who present with dyspnea, fever, and cough but no clear evidence of infection. We describe the clinical presentation, management, and response to rechallenge in one mantle cell lymphoma patient who developed R-ILD during maintenance rituximab. **Case report Case:** 66 years old male with history of mantle cell lymphoma (MCL), who had been treated with RCHOP and underwent autologous stem cell transplantation (ASCT), was diagnosed with relapse 5 years after ASCT. Six courses of rituximab-bendamustine resulted in 2nd complete response and 2-monthly rituximab maintenance was initiated. 10 days after 3rd rituximab, he presented with a 1 week history of progressive exertional dyspnea and cough. He was tachypneic and hypoxemic. **Methodology:** Thorax HRCT showed peripheral bilateral patchy ground glass opacities and nodular opacities. Bronchoalveolar lavage identified no bacterial, viral or fungal pathogen. With presumptive diagnosis of late R-ILD, methylprednisolone (MP) 1 mg/kg/day was started. In absence of rapidly progressing respiratory failure and fever, the patient was evaluated as non severe R-ILD. Thus, rechallenge with rituximab is being considered due to the risk of relapse of MCL. **Results:** Discussion: Reported rate of possible R-ILD is <0.03% in over 540,000 patients. Pulmonary complications of rituximab are hypersensitivity pneumonitis, ARDS, interstitial pneumonitis, organizing pneumonia, pulmonary fibrosis, and alveolar haemorrhage. Symptoms of R-ILD are dyspnea, fever, and hypoxemia and HRCT findings include focal alveolar densities, ground glass opacities and alveolar opacification. Time to symptom onset ranges from 1 day to several weeks after 1st infusion with mean **Conclusion:** mean duration of 3 months. Our patient had received rituximab prior to relapse and developed R-ILD after 9 doses of rituximab for relapse, which is a rare finding. All other causes of potential lung injury had to be meticulously excluded. ILD is a rare but potentially fatal pulmonary toxicity due to rituximab. As the symptoms at presentation are nonspecific, physicians must maintain a high index of suspicion to recognize it early and initiate treatment to avoid severe morbidity and mortality.

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PP 11

THE DIVERSITY OF PRESENTATION AND MANAGEMENT OF SUBCUTANEOUS PANNICULITIS –LIKE T-CELL LYMPHOMA WITH ASSOCIATED HEMOPHAGOCYTIC SYNDROME - CASE SERIES ANALYSIS

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**Objective:** Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare hematological malignancy affecting subcutaneous adipose tissue, typically with no involvement of the lymph nodes. SPTCL is associated with the increased risk of the hemophagocytic syndrome (HPS), significantly affecting prognosis and overall survival. This study aimed to present different clinical characteristics, management strategies, and outcomes in three patients diagnosed with SPTCL. **Methodology:** A retrospective study of the three patients diagnosed with SPTCL admitted to Hematology Departments in Krakow was conducted. Collected data included patients' clinical characteristics and symptoms, laboratory testing, imaging tests, implemented treatment strategies and response assessment. **Results:** The analyzed patients (aged 15-35), presented lesions involving mainly skin in 2 patients, and mesenterium in one subject; HPS was confirmed in each case. The first line treatment consisted of HLH protocols followed by next line chemotherapies in two patients, and then with high dose therapy in one case. Cyclosporine A (CyA) was implemented in two patients, and in one case this was an initial choice. CR was achieved in 2 patients, including the subject treated with CyA from the beginning. **Conclusion:** This series shows a diversity of presentations and implemented management in three patients. Since SPTCL is an extremely rare condition with no standardized established therapy, choosing the optimal treatment approach is a relevant problem. The increasing data shows the effectiveness and safety of immunosuppressive treatment with CyA versus intensive chemotherapy and supports the application of CyA also in patients with developed HPS.

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PP12

RELAPSED MANTLE CELL LYMPHOMA WITH ISOLATED CENTRAL NERVOUS SYSTEM INVOLVEMENT THAT TREATED WITH IBRUTINIB; A CASE REPORT AND LITERATURE REVIEW

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**Objective:** Mantle cell lymphoma (MCL) is an aggressive B-cell lymphoma, constitutes 3-10% of all non-Hodgkin's lymphomas. MCL usually presents with generalized lymph node involvement. The prognosis is poor and incurable. Extranodal involvement is not uncommon, but central nervous system involvement is very rare. Herein, we present a case with isolated central nervous system relaps who achieved a complete response with ibrutinib treatment. **Case report:** 53yearold female patient diagnosed with MCL underwent autologous stemcelltransplantation after R-CHOPchemotherapy. While being followed up in complete remission, she presented with a complaint of headache. Parenchymal lesions in brain was observed in MRI.Cerebrospinal fluid flow cytometric and cytological examination revealed MCL-centralnervoussystem involvement. There was no finding in terms of systemic relaps.The patient was achieved complete response with ibrutinib and high dose methotrexate **Results:** Central nervous system involvement at the time of diagnosis in mantle cell lymphoma is very rare however it can be more common in relaps and generally is associated with advanced stage disease or is a part of systemic relaps. Our case is quite interesting as it presents with isolated central nervous system infiltration. In this case, our treatment choice was ibrutinib because of its satisfactory response rates and proven effectiveness on central nervous system. **Conclusion:** The patient is currently being followed up with a complete response. It should be underlined that even in patients followed up with complete remission, symptoms such as headache, which can sometimes be subjective, should be approached sensitively, and it should not be forgotten that they may indicate an unexpected involvement of the disease.

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PP13

IS THERE ANY NEW PROGNOSTIC SCORE FOR PERIPHERAL T-CELL LYMPHOMA?

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**Objective:** To compare with IPI the usefulness of new prognostic scores in patients with peripheral T-cell lymphoma (PTCL) from a single institution. **Methodology:** Sixty patients (30 male/30 female) with PTCL [anaplastic large-cell lymphoma (ALCL) 18, PTCL not otherwise specified 32 and other 10]. International Prognostic Index (IPI), Modified Glasgow Prognostic Score (mGPS), Geriatric Nutritional Risk Index (GNRI), The combined index of hemoglobin, albumin, lymphocyte, and platelet (HALP), Platelet to Lymphocyte Ratio (PLR), Neutrophil to Lymphocyte Ratio (NLR), albumin/globulin ratio(A/G), Prognostic nutritional index(PNI) were calculated as in the original references. **Results:** mGPS,GNRI,HALP, PLR,NLR,A/G and PNI have not significance to predict overall survival in patients with peripheral T-cell lymphoma(Table-1). **Conclusions:** IPI is still superior from all prognostic scores (mGPS,GNRI,HALP,PLR,NLR,A/G and PNI) to predict overall survival.

Variables in the Equation

Table-1

	B	SE	Wald	df	Sig.	Exp(B)	95,0% CI for Exp(B)	
							Lower	Upper
IPI	0,598	0,167	12,75	1	0	1,818	1,31	2,525
mGPS	0,001	0,244	0	1	0,996	1,001	0,621	1,614
GNRI	0,014	0,017	0,738	1	0,39	1,014	0,982	1,048
HALP	0,036	0,275	0,017	1	0,897	0,965	0,563	1,655
PLR	0	0,001	0,166	1	0,684	1	0,998	1,003
NLR	0,035	0,046	0,599	1	0,439	1,036	0,947	1,133
A/G	0,399	0,463	0,74	1	0,389	0,671	0,271	1,663
PNI	0,008	0,014	0,357	1	0,55	0,992	0,965	1,019

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## MYELOMA

PP 14

**RISK ASSESSMENT FOR NEWLY DIAGNOSED, FIT AND YOUNG PATIENTS WITH MULTIPLE MYELOMA, IN THE ERA OF NOVEL TREATMENT MODALITIES: ARE THERE ANY ADDITIONAL FACTORS TO BE UNDER CONSIDERATION?**

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**Objective:** Multiple myeloma (MM) is considered a disease of elderlies however, 35-40% of newly diagnosed MM (NDMM) patients (pts) are ≤60 years (ys) old. Although young NDMM pts succeed better outcomes with the currently used treatment protocols, a considerable number of them (25-35%) succumb to MM, within 5 ys after diagnosis. We evaluated the

overall survival (OS) and the related risk factors, in NDMM pts aged ≤55 years and we designed a scoring system with predictive value on their long-term outcome. **Methodology:** Among 116 NDMM pts treated from 2010-20 in our center, 58 were ≤55 ys and 41% had advanced disease, 24% elevated LDH, 15% extramedullary disease (EMD) and 14% high-risk cytogenetic features. Following treatment with 3 (n=48) or 2 (n=10) agents of Velcade, Cyclophosphamide, Lenalidomide and DXM, 90% underwent autologous hematopoietic stem cell transplantation (AHSCT). Female gender, advance disease, EMD presence, elevated LDH and less than very good response pre-AHSCT, adversely affected the OS. **Results:** After a median follow up of 4 ys, the median OS was not reached however, approximately 25% of young NDMM patients died within 4 ys after diagnosis. Based on the aforementioned risk factors we created a risk scoring system which compared to the international staging system (ISS), sufficiently discriminated young NDMM patients who are at risk for poor outcome. The 4-year OS was superior for pts with 0-2 factors compared to those with 3-5 factors (86% vs. 44% respectively, p<0.001). **Conclusion:** Despite the current plethora of the available treatment agents, the heterogeneity in the outcomes among the NDMM pts, highlights the unmet need to establish appropriate criteria for personalized and more efficient treatment approaches, especially for the younger NDMM pts. In this study, we propose an easily applicable scoring system, which can discriminate younger NDMM pts who might need more intensive treatment aiming at prolonged survival rates.

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## PLATELET DISEASES

PP 15

**LONG-TERM OUTCOMES OF PATIENTS TREATED WITH CAPLACIZUMAB FOR IMMUNE-MEDIATED THROMBOTIC THROMBOCYTOPENIC PURPURA (ITTP): THE POST-HERCULES STUDY**

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**Objective:** The efficacy and safety of caplacizumab (CPLZ) for patients (pts) with immune-mediated thrombotic thrombocytopenic purpura (iTTP; also known as acquired TTP) were demonstrated in the Phase 3 HERCULES trial, with a 28-day follow-up period after end of treatment. Post-HERCULES (NCT02878603) evaluated the long-term outcomes of pts with iTTP treated with CPLZ during HERCULES, and the safety and efficacy of repeated CPLZ use for iTTP recurrence. **Methodology:** Over 3 years' follow-up, pts could receive CPLZ with therapeutic plasma exchange (TPE) and immunosuppressive therapy (IST) for iTTP recurrence. Safety was assessed during the overall study period in the intention-to-observe (ITO) population; TTP-related events (TTP-related mortality, recurrence, or major thromboembolic events) were assessed in pts without recurrence in HERCULES or prior to post-HERCULES (efficacy ITO population). Safety and efficacy were also evaluated during recurrences. **Results:** Of 104 pts enrolled, incidences of adverse events (AEs) were similar between pts treated with CPLZ +TPE+IST during HERCULES (n=75) and pts treated with TPE+IST only (n=29). TTP-related events occurred in 4/49 pts (8%) randomized to CPLZ vs 11/29 pts (38%) randomized to placebo. The first recurrence episode was resolved/resolving for all 13 pts treated with CPLZ for recurrence, including 9 pts with repeat CPLZ. The safety profile of CPLZ for recurrence was consistent with HERCULES. **Conclusion:** Over long-term follow-up, the safety profile of patients treated with CPLZ in combination with TPE+IST was generally similar to those who received IST+TPE only, with no observed increases in iTTP recurrence. Repeat use of CPLZ was efficacious, with no new safety concerns.

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## OTHER DISEASES

### PP 16

#### EFFICACY OF FUROSEMIDE IN METHOTREXATE CLEARANCE IN PATIENTS TREATED WITH HIGH DOSE METHOTREXATE

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**Objective:** Methotrexate was first used in 1947 as a chemotherapeutic drug in the treatment of acute lymphoblastic leukemia (ALL). Methotrexate has been extensively explored as an anticancer drug since that time. High dose methotrexate is a term used for doses above 1000mg/m<sup>2</sup>. The objective of this study is to determine efficacy of Furosemide in methotrexate clearance in patients treated with high dose methotrexate. **Methodology:** It was a prospective cohort study carried out at the Oncology department of a tertiary care hospital, Pakistan for a period of one year. Total 80 patients were enrolled and all received daily hydration of at least 5L along with urine alkalization with sodium-bicarbonate and calcium rescue as per protocol. All patients were given Furosemide 40 mg three times a day. Methotrexate levels were monitored every 24 hours to follow its clearance. Data analysis was done by using IBM SPSS version 24. **Results:** The mean (SD) hospital stay in the current study was 4 (±1) days. Frequency of delayed methotrexate clearance was observed in 16 (20%) patients. The mean (SD) time of methotrexate clearance was 4 (±1) days. Renal injury was observed in 8 (10%) subjects, electrolyte imbalance in 12 (15%) subjects, and transaminitis in 11 (13.75%) subjects while mucositis was observed in 8 (10%) subjects. **Conclusion:** Our study concludes that furosemide is effective in methotrexate clearance in patients treated with high dose methotrexate. The use of furosemide reduces the cost and hospital stay. As furosemide is cheaper and easily available so it can be used easily in the methotrexate clearance.

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### PP17

#### CART CELL THERAPY BLACK SHADOW IN HEMATOLOGICAL DISORDERS : SYSTEMIC REVIEW WITH META-ANALYSIS

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**Aim:** To determine the effect of CART therapy on hypogammaglobulinemia and bone marrow aplasia, and to determine the probable medications in management of hypogammaglobulinemia with other associated risk factors and complications. **Methodology:** Systematic search was conducted in 4

databases using the terms CART therapy, haematological malignancies, and hypogammaglobulinemia. Articles including patients with any haematological malignancies undergone CART therapy and assessment done on hypogammaglobulinemia were included. Following screening and selection of the articles, narrative synthesis, quality assessment, and meta-analysis were conducted **Results:** 1197 citations, 9 were finally included for meta-analysis comprising of 425 patients who were affected due to any haematological malignancies and had undergone CART therapy. The overall incidence rate was 35.35%. In all the studies, hypogammaglobulinemia was managed using IgG. Most of the patients across the studies had infection due to reduction in WBC count. The overall incidence of neutropenia following CART therapy was 59% lymphopenia was 82%, and B-cell aplasia was 49.5%. **Conclusion:** The effective way for management of hypogammaglobulinemia was using IgA antibody. The overall incidence of hypogammaglobulinemia and WBCs was difficult to conclude as majority of the studies were of low and fair quality and were collected at different time points after administration of CART therapy. Thus, good quality clinical trials, open label trials or RCT are required. Hypogammaglobulinemia increases with a decrease in neutrophils, lymphocytes, and B-type cells leading to variable infection.

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#### PP18

##### RECTAL CANCER DISTANCE TO THE ANAL VERGE AND THE T STAGING: MAGNETIC RESONANCE IMAGING FINDINGS

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**Objective:** This study sought to determine the magnetic resonance imaging (MRI) T staging and the rectal cancer (RC) distance to the anal verge in patients treated in radiotherapy department of Tripoli University Hospital. **Methodology:** An observational study was conducted in Radiotherapy department at Tripoli University Hospital retrospectively from January 1, 2018 to December 31, 2020 for total number of 73 patients whom met the inclusion criteria; 18-year-old or more, male and female with primary RC, T2 or more. distance metastasis or secondary RC were excluded. **Results:** Patients were 38 female and 35 male. Patient less than 50 years old was 25% and 38% was between 50-69 years old. patient at 70 years old or older was 10%. The low rectal cancer, less than 5 cm to the anal verge, is in 38.4% of the patients, with most of the patients at T2 staging (45.5%). While 19.2% was in the mid rectum, 5-10 cm to the anal verge, the T2 was 9%. Regarding the high rectum, more than 10 cm to the anal verge, it was

present in 42.5%, of which 45.5% was in T4b. **Conclusion:** Rectal cancer was less commonly in the mid rectum. in the low rectum it was commonly T2 stage and in high rectum T4b was predominant. Further studies are needed.

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#### PP19

##### A CASE OF FASCIOLOSIS PRESENTING WITH SEVERE HYPEREOSINOPHILIA

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**Objective:** *Fasciola hepatica* is a parasitic trematode and infects livers of various mammals and rarely infects human liver. Frequently eosinophilia is detected in laboratory findings, but it is generally mild or moderate as with other parasitic infections. Here we present a patient with Fasciolosis as the cause of severe hypereosiphilia. **Case report:** A 66-year-old female patient presented with weight loss, nausea and abdominal pain for one month. Her physical examination was unremarkable except for mild hepatomegaly. Her laboratory tests were as follows; leukocytes 29900/mm<sup>3</sup>, eosinophils 21550/mm<sup>3</sup> (%71.9), ALP 379 IU/L, LDH 278 IU/L, GGT 53 IU/L, CRP 30 mg/dl. All other etiological tests including primary secondary causes were negative. Abdominal MRI revealed focal patchy nodular lesions. *Fasciola hepatica* IHA (1/2560) was positive. **Results:** After the diagnosis, the patient was administered 2 doses of triclabendazole (10 mg/mg) at 5 day intervals. In the 3rd month of the treatment, the control eosinophil count decreased to 480/mm<sup>3</sup>, and the patient was free of any symptoms. **Conclusion:** Severe eosinophilia (>5000/mm<sup>3</sup>) is generally associated with malignant diseases, hypereosinophilic syndrome or primary hematologic disorders. But it would be useful to consider fasciolosis in hypereosinophilia patients who are sheep and cattle breeder and present with gastrointestinal system complaints such as jaundice and abdominal pain.

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#### PP 20

##### RITUXIMAB-INDUCED SEVERE ACUTE THROMBOCYTOPENIA IN A PATIENT WITH SPLENIC MARGINAL ZONE LYMPHOMA

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**Objective:** Rituximab, which is widely used in the treatment of B-cell lymphoma, is a chimeric monoclonal antibody directed against the CD20 antigen. Rituximab has many side effects, mainly allergic and neurological. Rituximab may cause thrombocytopenia in the long term after

administration. Rare cases with rituximab-induced acute thrombocytopenia have been reported in the literature. **Case report:** A 51-year-old female patient who newly diagnosed splenic marginal zone lymphoma received rituximab as first line therapy. Petechiae occurred in the lower extremities on the day following rituximab administration. The blood test showed a severe drop in the platelet count from 112,000/ $\mu$ L to 5,000/ $\mu$ L. Blood peripheral smear evaluation confirmed severe thrombocytopenia. **Results:** There was no change in hemoglobin or white blood cell levels. After the diagnosis of rituximab-induced acute thrombocytopenia, thrombocyte suspension was administered due to the risk of bleeding. Close clinical and laboratory observations were made. The platelet count began to rise gradually in the following period. Before the second week of rituximab administration, the platelet count was 122,000/ $\mu$ L. **Conclusion:** Rituximab has a widespread use, especially in malignancies and autoimmune diseases. Like many monoclonal antibodies, rituximab has several side effects. Thrombocytopenia is a long-term side effect associated with rituximab, and rituximab-induced severe acute thrombocytopenia has been rarely reported. Therefore, it should be kept in mind that severe acute thrombocytopenia may develop after rituximab administration.

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PP 21

#### VITAMIN B 12 DEFICIENCY MIMICKING THROMBOTIC MICROANGIOPATHY: A CASE REPORT

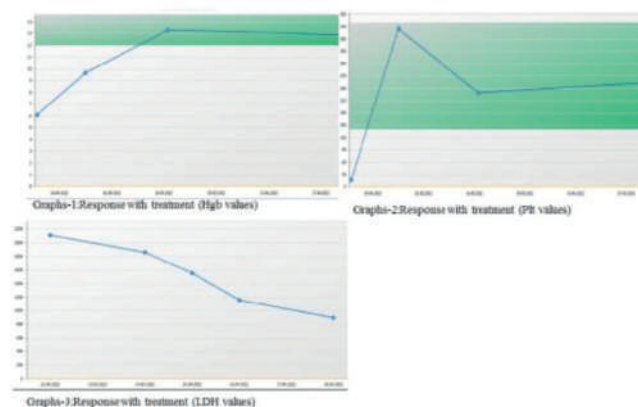
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**Objective:** Vitamin B12 has an important role in DNA synthesis, erythrocyte development and neurological functions by the transfer of one-carbon methyl groups. Vitamin B12 deficiency may mimic Thrombotic Microangiopathy (TMA) and lead to pseudo-thrombotic microangiopathy (pseudo-TMA). Early recognition of pseudo-TMA is important because treatment with vitamin B12 replacement is quite simple and effective. **Case report:** A 66-year-old female patient was admitted to the emergency department with complaints of fatigue. CBC values Hb 3.8gr/dL, Hct 11.3%, MCV 115 fL, platelets 19000/ $\text{mm}^3$ , WBC 6400/ $\text{mm}^3$ , ind.bil.1.5 mg/dL, LDH 2111U/L. In peripheral blood smear (PBS), macroovalocytes, anisopoikilocytes, schistocytes, hypersegmented neutrophils and a normoblast with megaloblastic features (figure-1) were observed. Thrombocytopenia and the presence of schistocyte initially supported TMA. **Methodology:** Blood was drawn from the patient for the ADAMTS-13 test. While concurrent steroid treatment with fresh frozen plasma (FFP) was started, plasmapheresis preparation was also made. The patient's vitamin B12 level was 50 pg/mL. The patient was started on vitamin B12

as 1000 mcg IM. Following clinical recovery, hemoglobin and platelets stabilized, the hemolysis panel indicated a steady improvement (graphs 1, 2, 3). **Results Conclusion:** TMA symptoms can be mimicked by severe vitamin B12 deficiency. Rapid and accurate diagnosis of pseudo-TMA and initiation of parenteral vitamin B12 replacement can prevent unnecessary and expensive diagnostic investigations and long-term plasma exchange treatments. Our case, has demonstrated the importance of considering vitamin B12 insufficiency in cases presenting with TMA and the value of carefully examining PBS in the identification of megaloblastic anemia.



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PP 22

#### QUALITY OF LIFE IN HEMATOLOGICAL PATIENTS IN THE POST-COVID ERA

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**Objective:** Currently, restrictions related to the COVID-19 pandemic have been lifted in many countries. However, the pandemic could still have impact on the current quality of life of patients, especially oncological ones. Our study aimed to determine the impact of the COVID-19 pandemic on the functioning of patients with hematological diseases. **Methodology:** This is a prospective survey-based study. We used the EORTC QoL questionnaire in the population consisting of 32 patients: 22 with lymphoma (69%), 4 with hairy cell leukemia (13%), 3 with myelofibrosis (9%), 1 with acute myeloid leukemia (3%), 1 with chronic myeloid leukemia (3%), 1 with non-oncologic disease (3%). The median age was 50.5 years (ranged 21 – 76). The questionnaires were collected between May and June 2022. Statistical analysis was performed using R software (R version 4.0.3.). **Results:** 41% of patients had a COVID-19 infection confirmed by PCR test. 38% of them were hospitalized, 80% of whom required oxygen therapy. Quality of life was 62.5 (16.7 – 83.3), functioning scales: physical

functioning 86.7, role functioning 66.7, emotional functioning 83.3, cognitive functioning 83.3, social functioning 66.7; symptom: fatigue 33.3, insomnia 33.3. Patients who required oxygen therapy had higher scores on the financial impact scale than those who didn't, 66.7 vs 0,  $p = 0.0261$ . **Conclusion:** Role and social functioning was the worst item among functioning scales. Women had significantly higher social functioning than men. Fatigue and insomnia were the most burdensome symptoms assessed on the symptom scales. No significant differences were found in scores of EORTC between patients who reported COVID infection and those who didn't. The limitation of this study is a relatively small research group. The future direction is to perform a similar analysis on a larger population.

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#### PP 23

##### ECULIZUMAB DOSE ADJUSTMENTS DURING PREGNANCIES IN PAROXYSMAL NOCTURNAL HEMOGLOBINURIA: A SINGLE CENTER EXPERIENCE.

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**Objective:** Paroxysmal nocturnal hemoglobinuria (PNH) has always been considered a relative contraindication for pregnancy. The use of eculizumab has reduced morbidity and mortality of fetus and mother. Dose adjustments are often required due to emerging breakthrough hemolysis, no standard recommendations are currently available in this setting. Here we report our single hematology center experience on breakthrough hemolysis and eculizumab dose adjustments during PNH pregnancies. **Methodology:** Clinical data of four pregnancies from three PNH patients are reported. Two of them were already on standard dosage eculizumab when pregnancies were diagnosed. Their baseline PNH clone sizes were 89.5% and 97.5% on granulocytes and 38% and 90% on erythrocytes, respectively. In both cases low molecular weight heparin-prophylaxis was started when pregnancy was diagnosed. The third 26 year old patient with a baseline PNH clone of 8.8% started treatment at the beginning of her 2<sup>nd</sup> trimester. **Results:** The 26 year old patient was stable on 900 mg Eculizumab until 12 weeks post-partum. The other two developed breakthrough hemolysis during their third trimesters. Eculizumab dosing was increased initially from 900mg

bi-weekly to 900 mg weekly and subsequently to 1200 mg biweekly. The 28 year old patient with the largest clone underwent two pregnancies and required even a 1200mg weekly dosage in her first pregnancy until four weeks post-partum. All four babies were delivered without complications. **Conclusion:** Eculizumab dose adjustments up to 1200 mg biweekly as well as interval shortening from bi-weekly to weekly administration seems effective and safe in breakthrough hemolysis control during pregnancy in PNH. Dose escalations did not impact on birth or development of the babies.

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#### PP 24

##### ALECTINIB-RELATED ERYTHROCYTE MEMBRANE CHANGES, NON-IMMUNE HEMOLYSIS AND ERYPTOSIS

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**Objective:** Alectinib is an anaplastic lymphoma kinase (ALK) inhibitor which standard initial treatment for patients with advanced ALK rearranged non-small-cell lung cancer (NSCLC). The current study was planned by the incidental observation of non-immun hemolysis signs in several alectinib-treated patients, and its aim was to comprehensively characterize erythrocyte changes under this drug. **Methodology:** We analyzed retrospectively 13 patients treated with alectinib for ALK+ NSCLC at the Bakirkoy Sadi Konuk and Kartal Dr Lutfi Kırdar Hospital Medical Oncology Department. Almost all patients were consulted with the hematology clinic because of anemia and elevated lactate dehydrogenase during alectinib. Laboratory tests requested for characterization of anemia included reticulocyte count, indirect bilirubin, haptoglobin, direct antiglobulin test, and LDH. All patients were examined by peripheral smear. **Results:** The analyzed patients, hematological tests results are showed that: Anemia was present in approximately all of patients and was mostly mild, (lowest hgb 8.5gr/dl). Reticulocytes were increased and the direct antiglobulin (Coombs) test was negative in all patients. Peripheral blood smears showed signs of eryptosis, abnormal red blood cell morphology in all patients, with anisocytosis, a predominance of acanthocytes, as well as occasional echinocytes, spherocytes, dacrocytes and rare fragmentocytes. **Conclusion:** We have reported 13 cases of significant alterations in erythrocyte morphology secondary to alectinib. Patients predominantly showed mild anemia, but one patient developed significant Coombs-negative hemolysis. In this case, hemolytic markers improved after alectinib was discontinued. This study highlights the need for both clinicians and haematologists to be observant for unrecognised off-target effects of novel agents.

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PP 25

**GLOMERULAR MICROANGIOPATHY WITH MARKED SYSTEMIC THROMBOTIC MICROANGIOPATHY SHORTLY AFTER BORTEZOMIB IN A NEWLY DIAGNOSED POEMS SYNDROME PATIENT**

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**Abstract:** The dipeptide boronic acid analogue bortezomib as a potent and selective inhibitor of the proteasome is used for the treatment of plasma cell dyscrasias such as multiple myeloma (MM). Bortezomib may induce glomerular microangiopathy (GMA) with or without systemic thrombotic microangiopathy (TMA) in which vascular endothelial growth factor-nuclear factor (VEGF) - $\kappa$  B pathway could be involved. MM itself can cause TMA but primarily at presentation. **Case report:** We present a case with GMA associated with clinical features supporting systemic TMA shortly after bortezomib. **Case:** A 54-year-old woman has been diagnosed as having POEMS syndrome. She had symmetric mild degree of peripheral neuropathy, sclerodermic skin lesions, Raynaud's phenomenon, and retinopathy. IgG kappa type paraproteinemia with a monoclonal increase of plasma cells and increased pulmonary artery pressure contributed to the diagnosis. Bortezomib based treatment was started. **Methodology:** At the 20th day she developed severe dyspnea. Bilateral pleural effusion and acute kidney failure with thrombocytopenia and microangiopathic hemolytic anemia were documented. Urgent steroid and plasmapheresis were started. ADAMTS13 level proved to be within normal and plasmapheresis did not contribute to improvement. She commenced on hemodialysis and kidney biopsy was decided. Light microscopy findings revealed glomerular capillary thrombus, basement membrane thickening and segmental **Results:** duplication. Hyperplastic arteriolar changes were present. No immune deposits were detected by immunofluorescence microscopy. Biopsy findings were diagnostic for thrombotic microangiopathy. The clinical picture deteriorated as sleepiness and confusion. Cranial imaging and cerebrospinal fluid analysis showed no abnormality. Eculizumab with off-label approval contributed to stabilization but no improvement. **Conclusion:** Conclusion: Proteasome inhibitors associated with TMA may be life-threatening along with organ dysfunction due to microangiopathy-related ischemia. Membrane attack complex (C5b-9) deposition was found on endothelial cells

in culture exposed to plasma from patients during the acute phase of the disease which may point to complement blockade benefit.

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**PEDIATRIC HEMATOLOGY ABSTRACT CATEGORIES**

**COAGULATION AND FIBRINOLYSIS DISORDERS**

PP 26

**THE SUCCESSFUL MAJOR SURGERY IN A PATIENT WITH INHERITED FVII DEFICIENCY AND A HUGE NASOPHARYNGEAL ANGIOFIBROMA**

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**Objective:** The bleeding phenotype of patients with inherited FVII deficiency is variable, and epistaxis is one of the most frequent symptoms. Interestingly, the bleeding risk does not correlate with the level of FVII activity. The severity of FVII deficiency and the type of surgery are not determinants of the optimal management of surgery, the doses and the duration of rFVIIa therapy are widely variable. The aim of this study is to present our successful experience in a 16-year-old boy with inherited FVII deficiency and a huge nasopharyngeal angiofibroma with a very high risk of bleeding **Case report:** The patient was referred with recurrent epistaxis in the last 6 months and he was diagnosed as an inherited FVII deficiency (FVIIC:29%, FVII inhibitor negative with positive family history). Tranexamic acid (10days) and rFVIIa (2doses) were used with success in the management of this surgery. Since this surgery may cause life-threatening bleeding, endovascular particle embolization was done to the important vessels feeding the mass one day before surgery without rFVIIa support. No bleeding or thrombosis were observed in our patient. **Conclusion:** In conclusion, a life-threatening major surgery was successfully done for a patient with inherited FVII deficiency and a huge angiofibroma. However, perioperative management of patients with FVII deficiency still remains a major challenge and clinical trials are needed to provide evidence-based optimal management of surgeries. And, angiofibroma should be thought in the differential diagnosis of epistaxis.

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## RED BLOOD CELL DISORDERS

PP 27

## ROLE OF SERUM HEPcidIN AND RETICULOCYTE HEMOGLOBIN CONCENTRATION IN EVALUATION OF ANEMIA IN ULCERATIVE COLITIS PATIENTS

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**Objective:** One of the most common extra-intestinal signs of ulcerative colitis (UC) disease is anemia, which has a considerable influence on patients' quality of life. **AIM:** The aim was to evaluate the role of serum hepcidin and reticulocyte hemoglobin concentration (CHr) in the study of anemia in UC patients. **Methodology:** We recruited 80 UC patients and 30 healthy individuals of matched age and sex as controls. Subjects were subdivided into three groups – Group I: 50 anemic UC patients, Group II: 30 nonanemic UC patients, and Group III: 30 healthy controls. **Results:** CHr showed a statistically highly significant decline in Group I than Groups II and III. Serum hepcidin showed a significant difference between Groups I, II, and III. Also, a significant negative correlation between CHr, serum hepcidin and severity of UC and a significant positive correlation between CHr and hemoglobin level, MCV, serum ferritin, and transferrin S. While serum hepcidin had a significant positive correlation with hemoglobin level, MCV, serum ferritin, transferrin S., and CHr. **Conclusion:** CHr had an excellent performance in prediction of iron-restricted anemia and was the test of best performance in prediction of iron-deficiency anemia ± ACD. Serum hepcidin had an excellent performance in prediction of ACD.

<https://doi.org/10.1016/j.htct.2022.09.1262>

## IMMUNODEFICIENCIES / NEUTROPHIL DISEASES

PP 28

## GRISCELLI SYNDROME TYPE 2 –CLINICAL APPROACH AND CASE REPORT

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**Objective:** Griscelli syndrome type 2 is rare autosomal recessive disorder caused by a defect in the RAB27A gene, which affects a melanosome-anchoring complex in melanocytes, affecting release of cytolytic granules from T and NK cells. Children with GS type 2 develop an uncontrolled T-

lymphocyte and macrophage activation syndrome known as hemophagocytic syndrome (HS) or hemophagocytic lymphohistiocytosis (HLH). We describe a 3 years old girl patient classic features of Griscelli syndrome type 2 **Case report:** A 3-year-old girl was admitted to hematology with complaints of LAP, hepatosplenomegaly and pancytopenia (WBC- 3080/ $\mu$ l, Hb-7.6 g/dl, Neutr.-350/ $\mu$ l, PLT - 165000/ $\mu$ l). The patient's condition was below the percentile, her skin was bronze, her hair was silver-grey. HLH criteria were met (triglycerides 458 mg/mL, ferritin 3445 ng/mL, fibrinogen 180 mg/dl). Morphology of the bone marrow was hypocellular, signs of dyserythropoiesis (stage I) and megakaryocytes were reduced **Methodology:** According to the clinical and laboratory data (hepatosplenomegaly, increased ferritin, hypertriglyceridemia, pancytopenia, hyperthermia resistant to antimicrobial therapy, silver-gray hair, pigment balls of hair seen light microscope) and the death of another undiagnosed child in the family, suggested likely primary HLH and GS. As a result of genetic analysis (homozygous mutation c.514\_518del-CAAGC(p.GLN172Asnfs\*,rs767481076)1 in the RAB27A gene), the diagnosis of GS type 2 was confirmed. **Results:** The patient was treated according to the HLH 2004 protocol. CSA levels were measured once a week. IVIG support was given based on IgG levels. HSCT was planned from patient's healthy HLA-matched sibling, but HSCT was delayed because the brother was infant. After 45 weeks of maintenance therapy, etoposide was discontinued, dose of dexamethasone was reduced to 5 mg/kg, but CSA was continued at the same dose. Control studies are carried out once a week. As far as possible HSCT is planning **Conclusion:** The prognosis of patients with Griscelli syndrome is poor. It is usually rapidly fatal within 1-4 years without aggressive treatment and bone marrow transplantation at onset of an accelerated phase. HSCT is more successful when implemented early course of the disease. Palliative care includes treatment and prophylaxis care infections and immunosuppressor therapy in accelerated phases. Some patients have died after transplantation, but others have had lasting remissions

<https://doi.org/10.1016/j.htct.2022.09.1263>

## LEUKEMIA

PP 29

## THE COURSE OF TOXIC HEPATITIS IN LEUKEMIC PATIENTS AT THE STAGE OF SUPPORT THERAPY.

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**Objective:** One of the main tasks in the treatment of acute leukemia is to prevent the development of complications of chemotherapy, as well as the timely choice of the correct tactics for the treatment of complications. Because forced breaks associated with complications negatively affect the end result

of leukemia treatment. Practice shows that one of the organs affected by chemotherapy is the liver, and its damage directly depends on the toxicity and duration of chemotherapy. Our task was to conduct research work in this area, and to study toxic liver lesions in patients with leukemia. Before that, we carried out similar work at the stages of induction and consolidation of treatment of acute leukemia in children. And this period of research work is devoted to the supportive stage of therapy in patients. **Objective:** To study the frequency of toxic liver damage in children with acute leukemia during support therapy, to choose treatment tactics according to the severity of toxic hepatitis. **Methodology:** The study group included 51 children with primary acute lymphoblastic leukemia who completed the induction stage with complete remission and retained this result for the entire period of consolidation. The age of the patients ranged from 2.5 years to 15 years. Of these, there were 28 boys and 23 girls. The patients were from Baku and the regions of the republic. Treatment of acute lymphoblastic leukemia was carried out according to two branches of the Moscow – Berlin – 2015 program: B and T ÍmRG. The protocols of maintenance therapy of these branches do not differ, and both begin with the 31st week of the general program, end on the 104th. Each protocol consists of 8 stages of a combination of chemotherapy drugs Metotrexat + 6-Mercaptopurine, which last for 6 weeks and alternate with two-week courses of reinduction - Deksametazon + Vinkristin. Before the start of maintenance therapy, all patients with leukemia confirmed the preservation of the previously achieved remission, and the functional and organic state of the liver. With positive results, the continuation of leukemia treatment began. And when the symptoms of toxic hepatitis were detected, the severity was determined. According to this indicator, 3 forms of flow were issued: light, medium-heavy and heavy forms. The tactics of conducting therapy of each form were chosen by us. **Results:** Of 51 patients, 42 had toxic hepatitis (82%). It was mild in 12 patients (23.5%), moderate in 26 children (50.9%), and severe in 4 children (7.8%). In the mild form of hepatitis, patients were prescribed intravenous administration of Riboksin + Aevit (orally) for 10-14 days, or alternatively, per os Ursobil + Aevit. This combination made it possible to restore all clinical and laboratory parameters in patients within 14-21 days, and at the same time, without interrupting chemotherapy. Moderate and severe forms of hepatitis occurred mainly during the period of reinduction (54.7%). The administration of intravenous ademetionine (Heptral) in the form of monotherapy for 8-12 days allowed continuous reinduction courses. Following him, the administration of an oral combination of Ursobil + Lipoic acid + Aevit for 14-21 days allowed to preserve the long-term effect. In severe hepatitis, chemotherapy was suspended, and patients were prescribed intravenous ademetionine (Heptral) in combination with oral Ursobil + Aevit for 10-14 days, and along with this detoxification therapy was carried out in parallel. Such treatment gave an improvement in clinical and laboratory parameters. Subsequently, intensive therapy was suspended, and chemotherapy was started accompanied by

Ursobil + Aevit + Lipoic acid for the next two weeks. This choice of therapy allowed us to preserve the restored indicators for a long time. There were no deaths or severe complications from toxic hepatitis in any case.

<https://doi.org/10.1016/j.htct.2022.09.1264>

#### HEMOGLOBINOPATHIES (SICKLE CELL DISEASE, THALASSEMIA ETC...)

PP 30

#### RARE UNSTABLE ALPHA GLOBIN VARIANT HBTAYBE (HBA1:C.118\_120DELACC) WITH HBA2 POLY A MUTATIONS, CAUSES TO HEMOLYTIC ANEMIA IN TWO CASES FROM AZERBAIJAN

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**Objective:** Sequence variants are usually silent and rarer in  $\alpha$ -globin, some may lead to an unstable protein with hemolytic or thalassemic phenotype. The most common HBA variant is ConstantSpring which is leading to an unstable elongated protein chain. Others may be due to ins/del in the  $\alpha$ -globin, one of them Hb-Taybe caused deletion of Thr residue at codon 40 of the HBA1. We report, for the first time, 2 cases with hemolytic anemia due to the presence of Hb-Taybe in *trans* with HBA2 poly-A mutations. **Methodology:** Patients were managed in the Thalassemia Unit of the National Hematology Center. Detailed pedigrees are drawn, medical recordings are reviewed and peripheral blood samples are collected. Sanger sequencing was performed with *in house* designed primers (HBA1, NM\_000558.5 and HBA2, NM\_000517.6) on genome analyser (ABI3500). Deletion and duplication analysis is performed by MLPA. **Results:** P-1: A 4-yr-old male who was diagnosed at the age of 1 yr with congenital hemolytic anemia. He presented with jaundice, the blood film showed moderate hypochromia and anisopoikilocytosis. He was transfusion dependent. P-2: A 45-yr-old female who was diagnosed at the age of 5 yr with congenital hemolytic anemia. She underwent splenectomy at the age of 32 yr due to moderate anemia. After splenectomy she was not transfusion dependent. Relevant clinical and laboratory data is presented at table. **Conclusion:** The clinical presentation is variable from mild hemolytic anemia to regular transfusion requirement. One patient had to have splenectomy in order to ameliorate the transfusion requirement. This study supports the requirement of  $\alpha$ -globin gene analyses, and a careful evaluation of cases with hemolytic anemia, particularly in populations where thalassemias are endemic, in order to avoid missing any of the rare globin variants and to offer accurate genetic counseling.

	P-1	P-2
Age at diagnosis (yr)	1	5
Consanguinity of parents	-	-
Spleen size below the left costal margin (cm)	3	underwent splenectomy
Cholelithiasis	+	-
Hb (g/dL)	6.1	8.4
RBC ( $10^6/\mu\text{l}$ )	2.93	3.01
MCV (fL)	76.8	108
MCH (pg)	20.8	27.9
Hb A2 (%)	1.7	1.7
Hb F (%)	6	0.1
Serum Iron ( $\mu\text{g/dL}$ )	113	149.9
Serum Ferritin (ng/ml)	115.8	1623
LDH (units/L)	-	554
Total bilirubin (mg/dl)	1.91	2.93
Direct Bilirubin (mg/dl)	0.62	0.76

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#### PP 31

##### HBH DISEASE AND SYSTEMIC LUPUS ERYTHEMATOSUS

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**Objective:** The association between thalassemia and systemic lupus erythematosus (SLE) is very rare. There are many articles in the literature showing that patients diagnosed with SLE with Beta-Thalassemia have a more severe hemolytic picture. The combination of Alpha thalassemia and SLE was first reported in an article published on January 30, 2021, by the staff of Guangzhou Hospital in the People's Republic of China. Our report is about combination of HbH disease and SLE, too. **Case report:** A 31-year-old female patient with HbH disease who had been irregularly monitored by a hematologist for 12 years received a blood transfusion for the first time during her 4th pregnancy and has not seen a hematologist since. At 12 weeks of gestation (7th pregnancy), a severe hemolytic anemic clinic was observed and erythrocyte mass transfusion was initiated. However, as different types of allergic reactions were observed during and after hemotransfusions autoimmune tests were held. **Methodology:** As a result, Direct Antiglobulin Test (DAT), Anti Nuclear Antibody (ANA), and anti-dsDNA positive, complement C3 levels were found below standard. The diagnosis of SLE was confirmed based on the fact that the patient's previous 6 pregnancies resulted in miscarriages and stillbirth. At a later stage, as a result of detailed instrumental and laboratory examinations, she was diagnosed with Lupus nephritis and steroid treatment was started under the control of a nephrologist. **Results:** Unit erythrocyte mass was transfused during cholecystectomy in this patient who was taken to the hospital with seizure pain in the right subcostal area that suddenly began at 22 weeks of gestation. 24-week pregnancy was ceased due to

intrauterine growth retardation. In the next month of follow-up, during the hospitalization 7 units of washed erythrocyte mass were transfused to the patient who was brought to the hospital with severe anemia after positive Covid-19 PCR analysis. **Conclusion:** In case published about the first patient with HbH disease and SLE it was reported an increase in the severity of anemia and the maintenance of Hb value in the range of 9.0-10.0 g / dl with steroid. According to our researchs there were found similarities between the outcomes of these two studies. Studies suggest that SLE patients with severe hemolytic clinics in regions with a high prevalence of thalassemia should be investigated for hemoglobinopathies.

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#### TRANSFUSION MEDICINE / APHERESIS / CELL PROCESSING

##### PP 32

##### EVALUATION OF CLINICAL AND LABORATORY FINDINGS OF THERAPEUTIC PLASMAPHERESIS IN CHILDREN

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**Objective:** Therapeutic plasmapheresis is an extracorporeal treatment method. The abnormal component of the patient's plasma is removed from the blood and replaced with the remaining blood components with a selected replacement fluid. We aimed to evaluate the demographic characteristics, procedure indications, procedure methods, differences between pre- and post-procedure laboratory parameters, and procedure-related complications of pediatric patients who underwent therapeutic plasma exchange (TPE). **Methodology:** Pediatric patients who underwent therapeutic plasmapheresis in Adana City Training and Research Hospital between 2018-2021 were included in our study. In this period, the number of pediatric patients who underwent therapeutic plasmapheresis was 61, and the total number of procedures was 238. The data of the patients were obtained from the files of the apheresis unit and the hospital registry system by retrospective analysis. Statistical analysis of the study was made with the SPSS v20 program. **Results:** 25 patients were female, 36 patients were male. Youngest patient was 6 months old and eldest was 17 years old. Patients weight range was between 5 and 104 kilograms. 191 of the procedures were TPE, 47 of them were lipid apheresis. The most common indications were hepatic failure, familial hyperlipidemia, neurological disorders, hematological disorders, sepsis with MODS and

intoxications. 119 transactions were in ASFA category-1. Complications were observed on 59 (%24,8) procedures. **Conclusion:** The most common complications are; vascular access related (obstruction) (21/59), hypotension (11/59), urticaria (7/59), technical malfunctions (7/59) and hypocalcemia (4/59). No exitus was observed due to the procedures. Therapeutic plasmapheresis procedure doesn't cause serious undesirable changes in laboratory values and serious complications are rare. Therapeutic plasmapheresis can be safely applied to pediatric patients in appropriate indications by making necessary adjustments.

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## PEDIATRIC ONCOLOGY ABSTRACT CATEGORIES

### LYMPHOMAS

#### PP 33

#### NON-HODGKIN'S LYMPHOMA: A RETROSPECTIVE ASSESSMENT OF CLINICAL FEATURES AND TREATMENT OUTCOMES

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**Objective:** The purpose of our study is to evaluate the demographic and clinical characteristics of pediatric Non-Hodgkin's Lymphoma (NHL) patients diagnosed and followed at our center, and also describe their survival rates and possible associations between outcomes and clinical features and to compare these data with the published reports from other clinical centers. **Methodology:** Children with NHL who were followed up and treated at Adana City Training and Research Hospital between 2013 and 2021 were included in the study. A total of 60 patients' files were collected and analyzed retrospectively. Age, gender, time of diagnosis, histopathological subtypes, primary location of the tumor, extranodal involvement, stage, bone marrow (BM) and central nervous system (CNS) involvement status, lactate dehydrogenase (LDH) levels at the time of diagnosis, type of chemotherapy, risk stratification, first line treatment response, localization of the radiotherapy if applied, relapse and survival outcomes were accessed from the files and analyzed. Patients with missing data in their files, patients who left the center without completing their treatment and patients who started treatment in another center and continued in our hospital were not included in the study. **Results:** The median age was 7 years (between 2-18 years) and the male/female ratio was 3.2. Burkitt's Lymphoma (48.5%) was the most common, Lymphoblastic Lymphoma (31.7%) was the second common histopathologic subtype and the primary site of the disease was abdomen in 34 patients (56.7%). It was seen that 28 of the patients (46.6%) had extranodal involvement, CNS involvement was only in 1 patient (1.6%) and bone marrow involvement was found in 13 patients (21.6%). It was determined that

80% of the patients were in the advanced stage (Stage 3-4) and complete remission was observed in 60.1% of the patients after the first line treatment. It was observed that the overall survival rate was 80.8%, and the event-free survival rate was 75% during the 96-month follow-up. Age, gender, primary site of the tumor, presence of extranodal involvement and stage did not have a statistically significant effect on overall and event-free survival. The effect of histopathological subtype on overall survival was found to be significant and highest survival rates were observed in B cell lymphoblastic and diffuse large B cell lymphoma. It was observed that the overall and event-free survival rate was significantly lower in the group with a LDH level above 500 U/L, which was measured at the time of diagnosis ( $p=0.01$  and  $p=0.008$ ). It was seen that the treatment response and both overall and event-free survival rates were found to be significantly higher in the groups with complete and partial response after the first line treatment ( $p<0.001$ ). The treatment-related mortality rate was found to be 45.4%, and the most common cause was febrile neutropenia/sepsis. **Conclusion:** Although childhood Non Hodgkin's Lymphomas have an aggressive nature and are detected in an advanced stage, survival results are good. It is very important to determine the risk groups to choose the appropriate intensive chemotherapy regimen and provide adequate supportive treatment for preventing treatment-related mortality and better outcomes.

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### SOFT TISSUE SARCOMAS

#### PP 34

#### SUCCINATE DEHYDROGENASE SUBUNIT B DEFICIENT PEDIATRIC GIST

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Case report Gastrointestinal stromal tumors (GISTs) occur exceedingly rare in children and adolescents. Eighty five percent of pediatric GISTs and 15 % of adult GISTs lack oncogenic mutations in KIT and PDGFRA. The results of tyrosine kinase inhibitor therapy in GIST cases with SDH deficiency are limited and controversial. Here, we would like to present a pediatric SDH deficient GIST case treated with surgery and Imatinib Mesylate. We obtained a good response with Imatinib Mesylate.

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PP 35

### SYNOVIAL SARCOMA ARISING IN THE RETROMOLAR TRIGONE: A RARE PRESENTATION

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Case report A 33-year-old female presented with complaints of lesion in the left retromolar trigone. CT scan demonstrated a soft tissue mass in left buccal space extending into the left infratemporal region. Biopsy was positive for Synovial Sarcoma. She received chemotherapy followed by wide local excision. Treatment with a total of 60 Gy radiotherapy was given. Patient tolerated the treatment well and remained disease free for 4.5 years. She developed recurrence and received palliative radiation for bleeding and pain control.

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### RARE TUMOURS AND HISTIOCYTOSIS

PP 36

### ASSOCIATION OF NF-1 AND MOYAMOYA SYNDROME : CASE REPORT

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**Introduction:** Neurofibromatosis type 1 (NF-1) is the most prevalent autosomal dominant genetic disorder. NF-1 vasculopathy is a significant complication of the disease. It affects both arterial and venous blood vessels of all sizes. Also Moyamoya syndrome is a cerebral vasculopathy. It is rarely detected with NF-1 in the pediatric group. Herein, we report of a 5 year-old male with NF1 and moyamoya syndrome. **Case Report:** A 6-month-old baby boy was brought by his family with the complaint of brown spots on the body. On physical examination, cafe au lait spots on the body, subcutaneous nodule in the occipital area and hypotonicity were found. He was examined considering neurofibromatosis, one of the neurocutaneous diseases. Abdominal ultrasonography, brain MRI, echocardiography, electroencephalography were normal. There was no pathological evidence in eye examination. In genetic tests, NF1 p.Gln2217 gene was found heterozygous

positive. patient was followed up with annual brain MRI. Hamartomatous lesions in left putamen and left thalamus posterior were detected in brain MRI when the patient was two years old. There was no pathological evidence on neurological physical examination. When he was three years old thickening and enhancement of the right optic nerve was found in MRI due to possible optic glioma. Only in the left cerebellar hemisphere, two millimeter-sized hamartomatous lesions in the white matter were found to have newly developed. Both internal carotid arteries (ICA) are thinned from the supraclinoid segment. Middle cerebral artery (MCA) M1 segment on the right and anterior cerebral artery (ACA) A1 segment on the left could not be selected. Many thin collateral vascular structures were selected in these localizations and were found to be significant in terms of Moyamoya disease. Regression was detected in right optic glioma. No predisposing factor was found in the examinations of the patient for thrombosis. Acetyl salicylic acid prophylaxis was started. The patient was taken under neurosurgery follow-up for revascularization surgery. The follow-up and treatment continues. **Conclusion:** Association of NF-1 and Moyamoya syndrome is rare, but carries a potential risk of clinicoradiological progression. Closed monitoring of children with neurofibromatosis type 1 enables early diagnosis of moyamoya syndrome. Revascularization surgery may effective way to prevent progression of clinical symptoms, but long-term results require close follow-up studies.

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PP 37

### EVALUATION AND MANAGEMENT OF THYROID NODULES AT A TERTIARY CARE PEDIATRIC CANCER CENTER IN TURKEY

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**Objective:** The object of this study is to search the characteristics of children and adolescents with thyroid nodules and analyze our institutional experience in the management of thyroid nodules. The complaints of these patients, physical examination findings, diagnostic features, results of radiologic researches, choice of the most appropriate modality to these patients' thyroid nodule assessment, and the management of the pathology results were revealed. **Methodology:** Patients who applied to the pediatric endocrinology or oncology outpatient clinic of Ankara City Hospital with the diagnosis of thyroid nodule were examined. All patients who has pathology result as benign, atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS), follicular neoplasm/ suspicious for a follicular

neoplasm (FN/SFN), suspicious for malignancy (SM), and malignant were searched. **Results:** A total of 130 patients presented with thyroid nodules. Female male ratio was 1,95:1. The youngest patient was 68 months old. At admission there was no goiter in 71.5% of the patients on physical examination. Of all patients 36% of them underwent fine needle aspiration biopsy and 8 of the 76 patients who underwent biopsy were diagnosed with papillary thyroid cancer. One patient diagnosed with follicular thyroid cancer Patients that diagnosed cancer, 4.6% of them treated with radioactive iodine. **Conclusion:** Although most pediatric thyroid nodules are benign, distinguishing benign from malignant lesions is crucial. Interdepartmental communication and competence are very important in the follow-up of patients with thyroid nodules. Because of an increased risk of cancer in the pediatric population, diagnostic and therapeutic procedures for pediatrics need further research including multicenter studies to attain universal consensus regarding the diagnosis and management.

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#### TUMOR BIOLOGY, IMMUNOLOGY AND IMMUNOTHERAPY

##### PP38

##### TRAMETINIB EXPERIENCE IN A BRAF P.N 486 \_P490DEL MUTATION POSITIVE LANGERHANS CELL HISTIOCYTOSIS

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Case report In Langerhans cell histiocytosis thyroid involvement is rarely seen. Here, we would like to present a 12-year-old male patient with lung, external auditory canal skin and

lymph node involvement in diagnosis. Disease relapse occurred with thyroid involvement 19 months after remission. In molecular analysis, BRAF p.N 486 \_P490del was detected and he received MEK inhibitor Trametinib monotherapy. He is still in remission for 16 months.

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##### PP 39

##### SERUM TOTAL OXIDANT AND ANTIOXIDANT STATUS IN CHILDREN WITH CANCER

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**Objective:** Oxidative stress has a potential role in carcinogenesis. Antioxidant enzymes have neutralizing effect both on cancer initiation, and progression. We aimed to assess the oxidant and antioxidant levels of pediatric cancer patients and to compare the levels in healthy controls. **Methodology:** The study involved 105 pediatric cancer patients (40 undergoing chemotherapy, 65 survivors) and 40 healthy children. The serum total oxidant status (TOS) and total antioxidant status (TAS) were measured. **Results:** The TOS and oxidative stress index were lower in pediatric cancer patients compared to the levels in the controls (3.73±1.35 vs. 4.21±1.72 μmol/L; p=0.08; 0.20±0.07 vs. 0.26±0.10; p=0.001, respectively). The mean serum TAS level was higher in patient groups compared to the level in the control (1.87±0.48 vs. 1.63±0.32 mmol/L, p=0.001). The TAS level of children with cancer in survivors was still found to be significantly higher compared to the levels in the control group (1.85±0.45 vs. 1.63±0.32 mmol/L, p=0.005). Radiotherapy, surgery, relapsed disease, presence of metastases and receiving enteral nutritional support caused no change in the TAS/TOS level. **Conclusion:** It has been revealed for the first time that the serum total antioxidant level increased during cancer treatment and didn't normalize after cessation of therapy for a long time.

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