Balkan Myeloma Study Group

Department of Clinical Therapeutics
National and Kapodistrian University of Athens
School of Medicine

HELLENIC REPUBLIC
National and Kapodistrian University of Athens
EST. 1837

EHOD

EUROPEAN HEMATOLOGY ASSOCIATION
Under the auspices of the EHA SWGMM

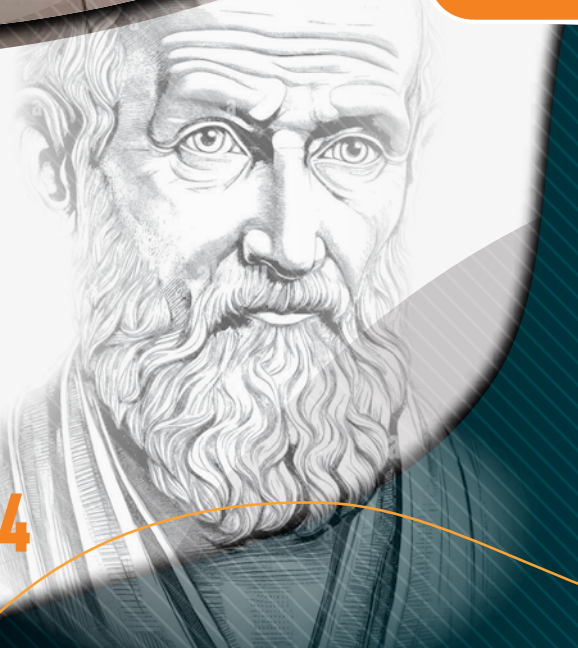
Abstracts Book

11th Aegean Hematology Oncology Symposium

AHOS 2024

19–22 September 2024

Kos | Kipriotis Village Hotel



www.ahos2024.com

DROMENA MEETINGS & EVENTS

LOVI Congress & Organization
Working Makes A Difference

BOOK OF ABSTRACTS

ORAL PRESENTATIONS

01. PHENOTYPES OF BONE MARROW MONOCYTES IN HEMATOPOİETİC CELL TRANSPLANTATION FOR ACUTE MYELOİD LEUKEMIA: A DESCRIPTIVE PILOT STUDY

Gül Yavuz Ermiş[1], Klara Dalva[2], Ekin Kırcalı[3], Şenay İpek[2], Nihal Okul[2], Güldane Cengiz Seval[2], Pervin Topçuoğlu[2], Selami Koçak Toprak[2], Meltem Kurt Yüksel[2]

[1]Health Sciences University Gülhane Training and Research Hospital Hematology Ankara, Turkey, [2]Ankara University Hematology, Ankara, Turkey, [3]Medicana Hospital Hematology, Ankara, Turkey

OBJECTIVE: In healthy individuals, 0-3% of BM aspiration consists of monocytes, more than 90% of are the classical type. Phenotypically, monocytes are classified in three different subsets according to the clusters of differentiation, they express: Classical M01 (CD14 bright/ CD16 -), intermediate M02 (CD14 bright/CD16+) and non-classical M03 (CD14 dim/CD16 +) by flow cytometry. In this series of acute myeloid leukemia (AML) patients, we aimed to investigate the relation of monocyte subsets and clinical outcomes of allotransplant recipients.

METHODS: We retrospectively investigated 38 AML patients who underwent allogenic stem cell transplantation (ASCT) in complete remission at Ankara University Hematology Department. Pretransplantation and the 28th day peripheral blood absolute monocyte numbers (AMNs) are categorised in three subgroups (<0.2, 0.2-0.95 and >0.95 X 109 /l) by total blood count and bone marrow (BM) aspirates monocyte percents and monocyte subsets by flow cytometry. Monoblasts are excluded in monocyte subsets. Stastistical analysis is performed with SPSS v.26 using Kaplan Meier, Mann Whitney U and Kruskall Wallis methods and used a significance level of 5%.

RESULTS: The demographics and details about transplants, flow cytometric analysis of pre and post- transplant BM aspirations and peripheral blood AMNs are evaluated. Median overall survival (OS) is 37.4 months, survival from ASCT is 12.3 months. Two years disease free survival (DFS) is 42%, DFS from ASCT in 12 months is 39%. Pretransplant peripheral blood AMNs and 28th day classical M01 subsets in de novo AML is significantly higher than secondary AML (p= 0.048). Three (7.8%) cases relapsed at 180th day and 15 (39.4%) cases suffered from grade 2-4 acute graft versus host disease, no differences both pre and posttransplant 28th days percentage, subsets of monocytes, peripheral AMNs. Primary engraftman failure (PEF) was found in three (7.8%) cases, 28th day monocyte percentage M01 subset (p=0.005) and 28th days peripheral AMNs (p=0.09) are lower, M02 (p=0.025) and M03 (p=0.005) subsets was higher than in PEF group. Transplanted related mortality (TRM) is detected in four (7.8%) cases, 100th, 180th and 365th day mortality is 7.8%, 26.3%, 42.1%, in all groups 28th day BM monocyte percentage was higher(p<0.05). Distribution of pretransplantation BM monocyte percentage in peripheral AMNs categories is significantly different (p=0.013). Conclusion: According to the literature most of the monocyte circulating in the first 7-10 days after transplantation (during pancytopenia) are the M03 however through the days 12th -28th days are the M01 subtype. In this pilot study there were no differences in the percentage of BM monocytes, monocyte subgroups, AMNs, grade 2-4 GVHD development, relapse and TRM. However in three patients who have PEF, both AMNs and M01 subgroup were low whereas M02 and M03 subgroups were high on the 28th day. BM monocyte percentage and subtypes may play a critical role in foreseeing PEF, but not agvhd, relapse and TRM. Prospective studies are needed to verify this hypothesis.

02. DETERMINATION OF MIRNA-133A AND MIRNA-452 EXPRESSION LEVELS IN CHRONIC LYMPHOID LEUKEMIA PATIENTS

Ayşe Dalyan[1], Mehmet Özaslan[1], Sibel Bayıl Oğuzkan[1], Mehmet Yılmaz[2]

[1]Gaziantep University, [2]Sanko University

OBJECTIVE: Chronic Lymphoid Leukemia (CLL), which constitutes a significant portion of leukemia cases, is a heterogeneous disease with highly variable prognostic features, defined by the accumulation of small, mature-looking B lymphocytes. miRNAs are a class of small non-coding RNAs that have critical roles associated with the occurrence and course of different malignancies, including CLL. Although miRNA-133a and miRNA-452 and their relationship with other cancer types have been determined, no study has been conducted on CLL. For this purpose, the expression levels of miRNA-133a and miRNA-452 were studied in CLL patients.
METHODS: The study included 63 patients diagnosed with CLL and 50 healthy individuals without a history of cancer as the control group. Quantitative Real-Time PCR (qRT-PCR) was used to analyze the expression levels of miRNA-133a and miRNA-452 in blood samples from CLL patients and the control group. Results: Our results revealed that the expression levels of miRNA-133a and miRNA-452 in the CLL patients were significantly decreased compared to the control group ($p<0.001$).
CONCLUSION: The downregulation in miRNA-133a and miRNA-452 expression levels in CLL patients compared to the control group suggests that these miRNAs may be new potential biomarkers in the early diagnosis of CLL. However, further research is needed to reach a certain conclusion. Acknowledgements: This study was approved by Gaziantep University Clinical Research Ethics Committee (Ethics committee approval number: 2021/163) and supported by Gaziantep University Scientific Research Projects Coordination Unit (Project No: FEF.DT.22.14).

03. RESULTS ON EFFICACY OF THE BV-AVD COMBINATION FOR ADVANCED STAGE CLASSICAL HODGKIN LYMPHOMA: A MULTICENTER REAL-LIFE EXPERIENCE FROM GREECE

Athanasios Liaskas[1], Maria Angelopoulou[1], Pinelopi Vryttia[2], Evgenia Verrou[3], Alexia Piperidou[1], Maria-Aikaterini Lefaki[1], Angeliki Georgopoulou[1], Alexandros Machairas[1], Dionisios Stoumbos[4], Georgia Kaiafa[5], Anastasia Sioni[6], Nikolaos Kanellias[7], Maria Arapaki[1], Elianna Constantinou[1], Dimitrios Gogos[8], Marina Siakantari[1], Eirini Katodritou[3], Panayiotis Panayiotidis[1], Sotirios Papageorgiou[2], Theodoros Vassilakopoulos[1]

[1]Department of Hematology and Bone Marrow Tranplantation, National and Kapodistrian University of Athens, Laikon General Hospital, Greece, [2]2nd Propaedeutic Department of Internal Medicine, "Attikon" General Hospital, [3]Hematology Department, Theagenio Cancer Hospital, Thessaloniki, Greece, [4]Department of Hematology, "Metaxa" Anticancer Hospital, [5]1st Propaedeutic Department of Internal Medicine, University General Hospital of Thessaloniki AHEPA, Aristotle University of Thessaloniki, [6]Department of Hematology, Agios Savvas Cancer Hospital, Athens, Greece, [7]Department of Clinical Therapeutics, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece, [8]Department of Hematology, "Vostaneio" Hospital of Lesvos, Greece

OBJECTIVE: Brentuximab Vedotin (BV) in combination with doxorubicin, vinblastine and dacarbazine (BV-AVD) has been approved for the first-line treatment of patients with advanced stage Hodgkin lymphoma (HL), based on the results of the ECHELON-1 study. Our aim was to describe the real-life experience with BV-AVD within a multicenter setting in Greece.

METHODS: Retrospective analysis of newly diagnosed patients with advanced HL according to GHSG (stages III/IV or IIB with mediastinal bulky disease and/or extranodal disease), who received BV-AVD treatment in 11 centers in Greece. iPET was evaluated according to Deauville 5-point scale and was considered as positive in cases with scores 4 or 5 (residual uptake >liver).

RESULTS: 57 patients were treated with BV-AVD (2 started with a half or one cycle of ABVD, and then continued with BV-AVD). The median age was 41 years old (range: 17-84; 23.6% of patients ≥ 60 years old) 57% were males, 82% had B-symptoms and 15% had bulky disease at diagnosis. By conventional staging, 70.9, 25.4 and 3.6% of the patients had disease stage IV, III and IIB respectively. 90% of the patients had stage IV disease based on baseline PET/CT. iPET was available in 50/57 patients and was positive in 6 (12%). All iPET+ patients had DS4 (SUVmax: 4.1-7.4) and no one switched to a different regimen. For iPET+ patients at the end of treatment (EoT): 2 patients were PET+ with DS4 but had complete remission and remain currently disease-free, 3 patients were PET-, 1 patient was already dead from an unrelated cause and only one had truly progressive disease and proceeded to salvage chemotherapy and autologous transplant. 2 deaths occurred during treatment including, one due to febrile neutropenia and one due to unrelated cause (myocardial infarction). Overall, there were 6 relapses, occurring between 7-43 months from treatment initiation, all derived from the iPET- population. With a median follow-up of 17 months, 2- and 3-year FFP was 88% and 82% respectively.

CONCLUSION: Our study provided comparable results to ECHELON-1 regarding treatment efficacy of BV-AVD. Due to the approved indication of BV-AVD, there was a predominance of stage IV in our study. iPET positivity was slightly higher in our study, but it did not compromise patients' outcome as the majority were either PET- or falsely PET+ at the EoT. Only 2 deaths occurred including one from unrelated cause. All relapses occurred in iPET- patients, implying that detection of prognostic factors in this subgroup of patients remains relevant even in the era of novel agents.

04. PROGNOSTIC EVALUATION OF PET/CT IN RESIDUAL POST-CHEMOTHERAPY +/-RT MASSES IN PATIENTS WITH HODGKIN LYMPHOMA AND ITS IMPACT ON SURVIVAL

Melis Bektaş[1], İrem Kar[1], Güldane Cengiz Seval[1], Selami Koçak Toprak[1], Pervin Topçuoğlu[1], Muhit Özcan[1], Önder Arslan[1], Taner Demirer[1], Meltem Kurt Yüksel[1]

[1]Ankara University Faculty of Medicine

OBJECTIVE: It is known that some patients have residue in PET-CT evaluation at the end of treatment, and no clear information about how follow-up should be done and duration. The aim of the study is to provide information about residual mass follow-up post-treatment.

METHODS: The present analysis was retrospectively conducted in 97 patients with negative PET at the end of the treatment, at our institution, from January 2005 to July 2024. All pts had disease evaluation performed also with CT scan. The location of the largest lymph node at diagnosis was grouped as location above and below the diaphragm and their size as <2.5cm, 2.6-5cm, 5.1-10cm, >10cm. The pts who received ABVD and RT or not. The mass size of those with residual mass at the end of treatment was monitored intermittently with CT until the last control or death. There were used with SPSS 27.0.

RESULTS: Main clinical characteristics: median age 35 years, males 67, B-symptoms 24, bulky disease 16, prior radiotherapy 31, relapsed 13 and dead 8. 56 pts in stage 1-2 and 41 in stage 3-4. In 73 pts, residual CT scan mass (PET-/CT scan +) of less than 2.5 cm in the diameter. Interim PET was performed in 55 pts. No significance was demonsrated between interim PET and end-of-treatment PET Deauville score, stage, number of chemo, relapse and residual mass size. The mean follow-up period of all pts was 38.7 months. The site of relapse was mostly in the iliac lymph nodes. No significance between it and the residual mass size, and the average duration was 24.1 months. According to the mass size at diagnosis, 55 pts end-of-treatment size remained the same, 39 pts decreased, 3 increased. The mean follow-up period was 37.5; 42; 17 months, respectively. That for stages 1-2 was longer than those for stages 3-4, 40.7;35.9 respectively. As the residual mass size increased, shortened in relapse time and overall survival. (p=0,023; p<0,001)

CONCLUSION:: In the majority of patients were early and intermediate stage, and yet the majority of patients had residual mass. Interim PET Deauville 2 and below, 70% of the patients did not relapse during follow-up. The importance of Interim PET evaluation is compatible with the guidelines. One patient with a residual size <2.5cm relapsed after 11 years, those with a residual size of 2.5-5cm after 34.2 months, and >5cm after an average of 23 months. Patients with Hodgkin lymphoma who have residual masses at the end of treatment should be followed up with CT for at least 3 years.

05. IPI 1-2 WITH BULKY DISEASE AND/OR VERY HIGH LDH DEFINES A HIGH-RISK SUBGROUP OF PATIENTS WITH PREVIOUSLY UNTREATED DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL): A HELLENIC DATABASE VALIDATION OF THE LEO COHORT

Theodoros Vassilakopoulos[1], Maria Arapaki[1], Sergios Tsakatikas[2], Evgenia Verrou[3], Christina Kalpadakis[4], Alexia Piperidou[1], Athanasios Liaskas[1], Sotirios Sachanas[5], Theodora Triantafyllou[3], Aikaterini Bitsani[1], Maria Dimou[1], Maria Ioakeim[1], Maria Siakantaris[1], Gerassimos Pangalis[5], Eirini Katodritou[3], Maria Angelopoulou[1], Vassiliki Pappa[2], Panayiotis Panayiotidis[1], Sotirios Papageorgiou[1]

[1]Department of Hematology and Bone Marrow Tranplantation, National and Kapodistrian University of Athens, Laikon General Hospital, Greece, [2]2nd Propaedeutic Department of Internal Medicine, "Attikon" General Hospital, [3]Hematology Department, Theagenio Cancer Hospital, Thessaloniki, Greece, [4]Department of Hematology, University of Crete, Iraklion, Greece, [5]Department of Hematology, Athens Medical Center, Psychikon, Greece.

OBJECTIVE: Maurer et al analyzed survival data for 1560 patients with DLBCL from the LEO cohort and defined High-risk International Prognostic Index (IPI) as the presence of either bulky disease (maximum tumor diameter (MTD) of ≥7cm) and/or very high LDH (LDH>1.3xULN) with an IPI score of 1-2. In the relevant study (AJH 2016), they identified a subset of IPI 1-2 patients with inferior outcomes similar to the ones of patients with IPI 3, consisting of roughly 50% of pts with IPI 1-2. This important finding warrants further validation. We aimed to validate the LEO cohort findings by analyzing survival data from the developing Hellenic database.

METHODS: Among 1529 DLBCL patients (pts) treated with immunochemotherapy (ICT) and included in our database, 1411 had full IPI data: 1235 aged ≤80 years old (yo) and 176 (12%) >80yo. Data on MTD were available in 1069/1411 pts (76%). Pts with IPI 1-2 were classified as "low-risk" (LR; LDH≤1.3x and MTD<7cm) or "high-risk" (HR; LDH>1.3x and/or MTD≥7cm). Freedom From Progression (FFP) was defined as the time between treatment initiation and death during treatment, primary refractoriness or relapse. Progression Free Survival (PFS) was defined as FFP plus death of any cause in first complete remission.

RESULTS: The median age of the 1411 pts was 67 years (IQR 56-75), 56% were males, 48% hade stage III/IV, 20% had PS≥2, 20% had ≥2 extranodal sites, 54% elevated LDH and 37% MTD≥7cm. As expected, IPI was highly predictive of FFP and PFS both in all pts and those ≤80yo. In pts ≤80yo the 2-year FFP was 94.1%, 87.7%, 74.1%, 69.8%, 50.7% and 44.0% for pts with IPI 0, 1, 2, 3, 4 and 5 respectively (p<0.001) with 2-year PFS rates roughly 1-3% lower. Pts with HR IPI1-2 (44% of all pts and 45% of those ≤80yo) had significantly inferior FFP and PFS compared to LR IPI 1-2. Roughly, in pts ≤80yo, the 2-year FFP of HR IPI1-2 pts was 71.8% vs 90.7% for LP IPI1-2 (p<0.001), being only 2% higher than that of pts with IPI 3. PFS data were similar. In addition, pts with IPI 2 had inferior 2-year FFP to those with IPI 1 (74.5% vs 89.4%, p<0.001 in pts ≤80yo). In multivariate analysis both HR IPI1-2 status and IPI 2 per se had independent prognostic impact with hazard ratios 2.32 and 2.42 respectively and p-values ≤0.001 for both.

CONCLUSION: Analysis of the Hellenic dataset confirms the findings published by Maurer et al with similarly sized LR and HR subgroups and numerically very similar 2-year PFS with the group of patients with IPI 1-2. Identification of a new subset of DLBCL patients with inferior prognosis not previously captured by current IPI variables is of great importance and warrants further attention. The Hellenic database is currently further enriched.

06. POLATUZUMAB VEDOTIN, RITUXIMAB, CYCLOPHOSPHAMIDE, DOXORUBICIN, VINCRISTINE, PREDNISONE (POLA-R-CHP) IN PREVIOUSLY UNTREATED PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL): A REAL-LIFE STUDY ACROSS 12 HELLENIC CENTERS

Theodoros Vassilakopoulos[1], Maria Arapaki[1], Georgia Kaiafa[2], Anastasia Banti[3], Evgenia Verrou[4], Theodora Triantafyllou[4], Maria Delatolla[5], Athanasios Liaskas[1], Christina Apostolopoulou[6], Athanasios Anastasiadis[3], Evangelos Makris[2], Chara Giatra[7], Vassileios Xanthopoulos[8], Aiketini Koutsi[9], Alexia Piperidou[1], Maria Ioakeim[1], Maria Siakantari[1], Panayiotis Panayiotidis[1], Eirini Katodritou[4], Maria Bouzani[7], Maria Angelopoulou[1], Sotirios Papageorgiou[6]

[1]Department of Hematology and Bone Marrow Tranplantation, National and Kapodistrian University of Athens, Laikon General Hospital, Greece, [2]1st Propaedeutic Department of Internal Medicine, University General Hospital of Thessaloniki AHEPA, Aristotle University of Thessaloniki, [3]Hematology Department, General Hospital "Papageorgiou GH", Thessaloniki, Greece, [4]Hematology Department, Theagenio Cancer Hospital, Thessaloniki, Greece, [5]Department of Hematology, Metropolitan General Hospital, Athens, Greece, [6]2nd Propaedeutic Department of Internal Medicine, "Attikon" General Hospital, [7]Department of Hematology and Lymphoma, Evangelismos General Hospital, Athens, Greece, [8]Department of Hematology, HYGEIA General Hospital, [9]Department of Hematology, Henry Dunant Hospital Center

OBJECTIVE: Based on the results of the POLARIX trial, which demonstrated the superiority of Pola-R-CHP over R-CHOP in terms of disease control, we aimed to evaluate the efficacy of Pola-R-CHP in previous untreated patients with DLBCL in a real-life setting across 12 centers in Greece.

METHODS: 74 patients with newly diagnosed DLBCL were included in our study. Based on the remarkable superiority of Pola-R-CHP over R-CHOP in patients with non-germinal center cell-of-origin (non-GCB COO) and those with International Prongostic Index (IPI) ≥3, many centers in Greece preferentially adopted this regimen as a new standard of care (SoC) in these subgroups, which were overrepresented. Patients >80 years old (yo) could still receive Pola-R-mini-CHP. Due to prohibitive cardiac comorbidities, gemcitabine replaced doxorubicin in 3 patients. Freedom From Progression (FFP) was defined as the time between treatment initiation and death during treatment, primary refractoriness or relapse. Progression Free Survival (PFS) was defined as FFP plus death of any cause in first complete remission.

RESULTS: The median age of the 74 pts was 72.5 years (range 23-89; 81% >60 yo and 24% >80 yo), 53% were males, 68% hade stage III/IV, 51% had B-symptoms, 45% had performance status (PS) ≥2 [including 18% with PS 3-4 (n=13)], 43% had ≥2 extranodal sites, 82% elevated LDH, 70% had anemia and 80% had a non-GCB COO. IPI was 1,2,3,4 and 5 in 10%, 13%, 35%, 28% and 13% respectively. Until now, 10 patients have died during treatment (13.5% - toxic deaths, early disease-related complications or progression; 8 with PS 2 and 2 with PS 4), 15 (20.3%) were primary refractory (stable or progressive disease at end-of-treatment evaluation or earlier) and 1 (1.4%) experienced a relapse. The 2-year FFP for the whole cohort was 56% with no difference for patients ≤80 and >80 yo. Impaired PS was an extremely unfavorable prognostic factor with 2-year FFP of 80% vs 19% for PS 0-1 vs ≥2 (p=0.001). B-symptoms also predicted for a lower 2-year FFP (66% vs 45%, p=0.02). No other prognostic factors could be demonstrated in our study. Very high IPI (4-5) and non-GCB COO were associated with numerically but not statistically inferior FFP.

CONCLUSION: Our study demonstrates our real-life experience with Pola-R-CHP, however in a rather negatively selected unfavorable population with untreated DLBCL. Pola-R-mini-CHP was safe and effective in very elderly patients (>80 yo), who were excluded from POLARIX. The efficacy of Pola-R-CHP was limited in patients with impaired PS (45% of all patients vs 16% in POLARIX, including 19% PS 3-4 who were ineligible for POLARIX). This was implied by the increased percentage of early deaths as a result of selection of patients with very unfavorable profile. The Hellenic database is currently further expanded in order to define the patterns of selection of patients for Pola-R-CHP and investigate the outcomes in the real-life in specific patient subgroups.

07. INVESTIGATION OF POTENTIAL GENETIC MECHANISMS IN PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

Kutay Bulut[1], Bahar Sevgili[2], Zühal Demirci[2], Fatma Keklik Karadağ[3], Fahri Şahin[2], Güray Saydam[2], Sunde Yilmaz Süslüer[1]

[1]EGE University/Medical Biology, [2]EGE University/Hematology, [3]Izmir Health Sciences University/Hematology

OBJECTIVE: The aim of this study is to elucidate the molecular mechanisms underlying the rare disease of Paroxysmal Nocturnal Hemoglobinuria (PNH) and to clarify more data on this patient group and to investigate the expression levels of some genes responsible for DNA methylation, which are thought to be associated with PNH disease and mutations have been found in previous studies after a literature search. Based on the view that the expression levels of genes responsible for some genomic rearrangements that are likely to play a role in the molecular pathogenesis of PNH rare disease may be unique markers in diagnosis, the hypothesis of the study is to understand the possible contributions to the diagnosis and/or treatment of diseases and their adaptability to the clinic. Methods: In this study, total RNA was isolated from whole blood samples obtained from 21 PNH patients diagnosed from patients admitted to the Department of Hematology, Ege University Faculty of Medicine, and from healthy volunteers as a control group, and its quantity and purity were determined using spectrophotometric method for quality control. Expression levels of relevant genes (DNMT3A, ASXL1, TET2, EZH2, RUNX1, IDH1, PIGA, PHF6, U2AF1, ATM) were determined using qRT-PCR method. Quantitative evaluation of gene expressions was performed by ΔΔCT analysis using the housekeeping gene (GAPDH) ratio. After quantitative evaluation, the gene expression levels of the patient group were compared with the gene expression levels of the control group in order to understand the possibility that the expression levels of the relevant genes may be unique markers in diagnosis, their adaptability to the clinic, and their possible contribution to the diagnosis and/or treatment of diseases. ΔΔCT statistical analysis was performed and the results were expressed as mean ± standard deviation. Fold change graph was used to visually analyze the results. $p<0.05$ was considered significant.

RESULTS: DNA methylation-related DNMT3A gene showed 1.04-fold overexpression, ASXL1 gene 15.30-fold overexpression, TET2 gene 1.57-fold overexpression, IDH1 gene 0.86-fold expression decrease and EZH2 gene 1.87-fold overexpression. 0.15-fold expression decrease in the disease-related PIGA gene, 3.58 overexpression in the transcription-related RUNX1 gene, 2.38 overexpression in the PHF6 gene, 3.43 overexpression in the DNA repair-related ATM gene, and 3.94 overexpression in the RNA splice-related U2AF1 gene were detected.

CONCLUSION: According to these results, overexpression was observed in most of the methylation-related genes and especially the overexpression in ASXL1 gene suggests that this gene may play an important role in the diagnosis and treatment of the disease.

08. PROGNOSTIC SIGNIFICANCE OF SERUM BLYS AND SOLUBLE BCMA (SBCMA) LEVELS IN MULTIPLE MYELOMA

Annita-Ioanna Gkioka[1], Alexandros Alexandropoulos[1], Alexandros Gkiokas[1], Mavra Papadatou-Gigante[1], Aspasia Koudouna[1], Thommais -Marina Tryfou[1], Vasiliki Bartzi[1], Marie-Christine Kyrtsonis[2]

[1]Hematology Section, First Department of Propedeutic Internal Medicine, Laikon General Hospital, Athens, Greece, [2]First Department of Propedeutic Internal Medicine, Laikon General Hospital, National and Kapodistrian University of Athens,

OBJECTIVE: B-cell maturation antigen (BCMA), a member of the tumor necrosis factor receptor superfamily, is expressed preferentially from the late stages of B-cell maturation until differentiation of plasma cells. BCMA can be cleaved from B cells and circulated as a soluble factor (sBCMA). It serves as one of three receptors for B-lymphocyte stimulator (BLyS). In MM, BLyS promotes cell adherence and survival by a paracrine mechanism. sBCMA is currently of close consideration due to drugs that work against it. The purpose of this study was to investigate the prognostic significance of both serum BLyS and sBCMA in MM, as well as the potential relationships between these two molecules with clinical features.

METHODS: We studied 101 MM patients at the time of diagnosis until last follow up or death; Medical records were reviewed after patients' informed consent was obtained. Patients' sera, drawn at diagnosis and samples from 20 healthy individuals, were kept frozen and retrospectively analyzed. Serum BLyS and sBCMA were measured by commercially available ELISA kits, according to the manufacturer's instructions (Duoset kit R&D System). Patients' median BLyS and sBCMA levels, was used as a cut-off point in survival analysis. P value <0.05 was considered statistically significant. Statistical analysis was performed using the SPSS v29.0 software.

RESULTS: The median age of patients was 67 years (range, 31-90) with 55 (54.5%) patients men and 46 (45.5%) women. Ig type was IgG in 60 (59%) patients, IgA in 25 (25%) patients, light-chain in 13 (13%) patients, IgD and biclonal in 3 (3%) patients, respectively. As ISS 1, were staged 31 (32%) patients, ISS 2, 29 (30%) and ISS 3, 37 (38%). Median overall survival of the patients was 70 months (range, 1-315). Median level of serum BLyS ranged from 14 to 24785 pg/ml with a median 360.9 pg/ml and sBCMA ranged from 18 to 509.624 pg/ml with a median value of 904.5 pg/ml. In normal controls serum BlyS levels were 81pg/ml (range, 14-995) and sBCMA were 160 pg/ml (range, 70-1030), respectively. Significant correlation between serum BLyS and sBCMA was observed (r=0.426, p=0.0008). Overall survival was improved in patients with increased sBCMA/BLyS ratio (p=0.024). Among disease characteristics, serum BLyS levels correlated with immunoparesis (r= -0.260, p=0.013) and response ≥PR (r= 0.210, p=0.036) and did not correlate with ISS, serum albumin ≤3.5 g/dl, abnormal Karyotype, abnormal LDH, Response, Calcium≥10.5g/dl, FLCR≥100, Bone Marrow Infiltration≥60%, Platelets≤100.000/μl, Creatinine≥2 g/dl, Beta-2 Microglobulin. sBCMA levels correlated with bone disease (r= 0.369, p=0.001), Immunoparesis (r= -0.216, p=0.04), albumin ≤3.5 g/dl (r=-0.203, p=0.045), Hb ≤10 g/dl (r=0.222, p=0.027). No correlation was observed between serum sBCMA and ISS, serum albumin ≤3.5 g/dl, abnormal Karyotype, abnormal LDH, Response, Bone disease, Calcium≥10.5 g/dl, FLCR≥100, Bone Marrow Infiltration≥60%, Platelets≤100.000/μl, Creatinine≥2 g/dl and Beta-2 Microglobulin.

CONCLUSION: sBCMA and BLyS correlate with important disease parameters in MM. Serum sBCMA/BLyS ratio is an independent prognostic factor for overall survival in MM patients. This association appears to contribute novel knowledge and further investigation would be beneficial.

09. DISCONTINUATION OF LENALIDOMIDE MAINTENANCE AFTER ASCT IN MULTIPLE MYELOMA BASED ON SUSTAINED MRD NEGATIVITY FOR THREE YEARS: RESULTS FROM A PROSPECTIVE COHORT STUDY

Panagiotis Malandrakis[1], Ioannis Ntanasis-Stathopoulos[1], Ioannis V Kostopoulos[2], Vasiliki Spiliopoulou[1], Despina Fotiou[1], Foteini Theodorakakou[1], Magdalini Migkou[1], Nikolaos Kanellias[1], Evangelos Eleutherakis-Papaiakovou[1], Efstathios Kastritis[1], Maria Gavriatopoulou1, Ourania Tsitsilonis[2], Meletios-Athanasios Dimopoulos[1], Evangelos Terpos[1]

[1]Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece, [2]Department of Biology, School of Science, National and Kapodistrian University of Athens (NKUA), Athens, Greece

OBJECTIVE: Utilizing advanced techniques, such as next-generation flow (NGF) cytometry and PET/CT in order to asses if sustained minimal residual disease (MRD) negativity for three years can guide discontinuation of lenalidomide maintenance.

METHODS: NDMM patients were prospectively included from January 1, 2016, to December 31, 2021, who underwent ASCT followed by lenalidomide maintenance. MRD status was assessed in patients who achieved sCR at 6, 12, 24, and 36 months after starting maintenance. Samples were evaluated with NGF according to the EuroFlow protocol. Patients who had at least three consecutive MRD-negative results and received a minimum of 36 months of maintenance therapy underwent a PET/CT scan. If these patients also achieved imaging MRD negativity, they discontinued lenalidomide maintenance and MRD assessments were conducted every 6 months thereafter. If a patient converted from negative to positive or relapsed from sCR, lenalidomide maintenance was resumed at the same dose level.

RESULTS: Overall, 194 patients received induction therapy with proteasome-inhibitor based regimens (VCD, VRD, or VTD) and underwent ASCT. During a median follow-up of 63.5 months (range 6-104) from diagnosis, 49 patients (25.2%) experienced disease progression and 20 (10.3%) died. During this period, 51 patients (26.3%) achieved sustained bone marrow and imaging MRD negativity at 3 years after starting maintenance, leading to the discontinuation of lenalidomide. The median age at MM diagnosis for this subgroup was 56 years (range 39-66), with 27 (53%) being male. The patient distribution by ISS was 66.6% in ISS-1, 19.6% in ISS-2, and 13.8% in ISS-3, and by R-ISS was 60.8% in RISS-1, 33.3% in RISS-2, and 5.9% in RISS-3. Additionally, 31% of this subgroup had at least one high-risk cytogenetic factor. The median follow-up period from maintenance discontinuation was 32 months (range 4-52). The percentages of patients who remained MRD negative after discontinuing maintenance at 6, 12, 18, 24, and 30 months were 96% (48/50), 95.1% (39/41), 97% (37/38), 94.4% (34/36), and 92% (23/25), respectively. Three years post discontinuation, 12 out of 14 patients (86%) were MRD negative, and at 42 and 48 months all evaluable patients (8 and 4, respectively) remained MRD negative. Overall, 11 patients restarted lenalidomide monotherapy after converting from MRD negative to positive; four of these patients progressed and received second-line treatment. For these patients, the median follow-up time from the re-initiation of lenalidomide was 7 months (range 0-35 months) and the median time to progression for those who progressed was 9.5 months (range 1-26 months). The median progression-free survival (PFS) was 74 months (95% CI: 38-104 months). Only one patient who discontinued maintenance died from causes unrelated to MM. Conclusion: Sustained MRD negativity after ASCT and a completion of 3 years of lenalidomide maintenance may guide the safe discontinuation of maintenance, although this has to be proven in prospective randomized clinical trials. Close follow-up with consecutive MRD testing can trace an early myeloma relapse and the reinitiation of lenalidomide in relapsed patients could possibly delay disease progression.

10. ISATUXIMAB WITH POMALIDOMIDE AND DEXAMETHASONE IN PATIENTS WITH RRMM AT FIRST RELAPSE WITH PRIOR LENALIDOMIDE EXPOSURE: A PHASE 2 STUDY OF THE GREEK MYELOMA STUDY GROUP

Ioannis Ntanasis-Stathopoulos[1], Maria Gavriatopoulou[1], Alexandros Spyridonidis[2], Emmanouil Spanoudakis[3], Anastasia Sioni[4], Eirini Katodritou[5], Eleftheria Hatzimichael[6], Maria Kotsopoulou[7], Nikolaos Giannakoulas[8], Nasia Antoniou[9], Nikolaos Kanellias[1], Anastasia Pouli[4], Efstathios Kastritis[1], Meletios-Athanasios Dimopoulos[1], Evangelos Terpos[1]

[1]Department of Clinical Therapeutics, Alexandra General Hospital, National and Kapodistrian University of Athens, Athens, Greece, [2]Hematology Division, Department of Internal Medicine, University of Patras, Medical School, Patras, Greece, [3]Department of Hematology, Democritus University of Thrace Medical School, Alexandroupolis, Greece, [4]Hematology Department, "St Savvas" Oncology Hospital, Athens, Greece, 5Department of Hematology, Theagenio Cancer Hospital, Thessaloniki, Greece, [6]Department of Hematology, Faculty of Medicine, University of Ioannina, Ioannina, Greece, [7]Department of Hematology, Metaxa Cancer Hospital, Piraeus, Greece, [8]Department of Hematology of University Hospital of Larisa, Faculty of Medicine, University of Thessaly, Larisa, Greece, 9Health Data Specialists, Dublin, Ireland

OBJECTIVE: To report preliminary results from the EAE115 study, which investigates the efficacy and safety of IsaPomDex in patients with multiple myeloma (MM) experiencing their first relapse after treatment with a lenalidomide-containing regimen.

METHODS: EAE115 (NCT05298683) is an investigator-initiated, phase 2, prospective, open-label, multicenter study currently underway in Greece, aiming to enroll 108 adult RRMM pts who have received only one prior line of treatment containing lenalidomide and a PI. Patients must also have sufficient bone marrow and liver function and an Eastern Cooperative Oncology Group performance status (ECOG PS) of 2 or less. Pts who have received previous anti-CD38 mAb therapy, Pom or stem cell transplantation within 12 weeks prior to treatment initiation are excluded. Pts initially receive six 28-day cycles of Isa 10 mg/kg IV (once weekly [QW] in cycle 1, then every two weeks [QW2]) plus Pom 4 mg/day PO (days 1-21) and Dex 40 mg (or 20 mg if ≥75 years) PO/IV (QW). Thereafter, pts achieving at least very good partial response (VGPR) are randomized 1:1 to receive Isa QW2 or QW4 plus PomDex, while pts achieving <VGPR continue treatment with Isa QW2 plus PomDex. The study primary endpoint is the 6-month overall response rate (ORR; defined as partial response [PR] or better) to IsaPomDex.

RESULTS: As of 31 May 2024 (data cut-off), 39 patients had received ≥1 dose of IsaPomDex and thus are included in this analysis. Of these, 24 (61.5%) pts were still under treatment and 15 (38.5%) had discontinued due to progressive disease (8 pts; 20.5%), death (4 pts; 10.3%), consent withdrawal (2 pts; 5.1%) or physician's decision (1 pt; 2.6%). The median age at baseline was 72.0 years (range 60.0-87.0), with 24 (61.5%) pts being male. Thirty-seven (94.9%) pts had ECOG PS ≤1, 19 (48.7%) pts had stage I and 17 (43.6%) stage II disease as per the revised International Staging System (R-IIS), 8 (20.5%) had high-risk cytogenetics, 19 (48.7%) had lytic bone lesions and 3 (7.7%) had soft-tissue plasmacytomas. Twenty-seven (69.2%) pts had achieved ≥VGPR in the previous line, while 8 (20.5%) had undergone autologous stem cell transplantation (ASCT). At a median follow-up of 7.4 months (range 0.7-19.0), pts have reached a median of 7 cycles of IsaPomDex (range 1-20), with 23 (59.0%) pts having completed ≥6 cycles. Among 34 response-evaluable pts, the ORR was 73.5% with 29.4% achieving ≥VGPR. The median time to first response was 1.0 month (range 0.9-13.8). Thirty-three (84.6%) pts experienced ≥1 treatment-emergent AE (TEAE) and 14 (35.9%) ≥1 serious TEAE. Grade ≥3 TEAEs occurred in 25 (64.1%) pts, with neutropenia being the most common (18 pts; 46.2%). Conclusion: In this preliminary analysis, IsaPomDex demonstrated promising clinical activity, with rapid responses in pts at first relapse following treatment with a lenalidomide-containing regimen. The safety of IsaPomDex was consistent with the known safety profile of this combination.

11. PREDICTIVE AND PROGNOSTIC VALUE OF OCULAR ADVERSE EVENTS IN NEWLY DIAGNOSED PATIENTS WITH MULTIPLE MYELOMA TREATED WITH BELANTAMAB MAFODOTIN; A SUB-ANALYSIS OF THE BELARD STUDY

Maria Gavriatopoulou[1], Ioannis Ntanasis-Stathopoulos[1], Panagiotis Malandrakis[1], Despina Fotiou[1], Magdalini Migkou[1], Foteini Theodorakakou[1], Vasiliki Spiliopoulou[1], Rodanthi Syrigou[1], Evangelos Eleutherakis-Papaiakovou[1], Giorgos Psarros[2], Efstathios Kastritis[1], Meletios-Athanasios Dimopoulos[1], Evangelos Terpos[1]

[1]Department of Clinical Therapeutics, Alexandra General Hospital, National and Kapodistrian University of Athens, Athens, Greece, [2]Health Data Specialists, Dublin, Ireland

OBJECTIVE: To present data from the BelaRd study, evaluating Belantamab mafodotin (belamaf; GSK2857916) plus lenalidomide/dexamethasone (Rd) in transplant-ineligible pts with newly diagnosed MM, that offer insights on the association between ocular adverse events (OAEs) and belamaf's clinical activity.
METHODS: The ongoing phase 1/2 BelaRd study (NCT04808037) is comprised of 2 Parts. Part 1 evaluates the safety/tolerability of three different belamaf doses (2.5/1.9/1.4 mg/kg) plus Rd. Part 2 assesses the safety/efficacy of RP2D in Groups A and B and evaluates two belamaf dosing guidelines for managing OAEs. We present safety/efficacy results over an extensive follow-up period for both Parts (cut-off date 15/05/24).
RESULTS: This analysis includes all patients (pts) from both Parts of the trial who have completed three cycles of treatment (n=65; median age: 74.0 years; male: 38 [58.5%]), of whom 49 (75.4%) are still on treatment and 16 (24.6%) discontinued (11 [16.9%] fatal events; 3 [4.6%] consent withdrawal; 2 [3.1%] progressive disease). The interval between the first belamaf dose and the first manifestation of a Gr≥2 OAE varied greatly among pts and can be used to divide them into two hypothetical groups. The first group consists of pts who had a Gr2-4 OAE within the first three months of treatment (Group 1; 19/65, 29.2%). The second group consists of pts who only had Gr0-1 OAEs during this time (Group 2; 46/65, 70.8%). By the CCO date, 68.4% of Group 1 pts had achieved a ≥CR response, while the respective proportion in Group 2 was 37.0%. Importantly, this trend was observed across all three dose levels of this analysis. The proportions of ≥CR responses were 100%, 57.2% and 100.0% for Group 1 and 57.2%, 28.6% and 45.5% for Group 2 for the dose levels of 2.5, 1.9 and 1.4 mg/kg, respectively. Additionally, for Groups 1 and 2, the median (range) from the 3-month landmark time to CR in months was 11.76 (4.37-13.90) and 23.29 (8.67-NR), respectively. The median (Q1-Q3) duration of the interval between belamaf doses was 13.1 (10.3-18.6)/11.9 (8.0-13.3) weeks for Groups 1 and 2, respectively, while the respective belamaf cumulative dose intensities were 0.543/0.625 mg/month. Finally, at a median follow-up of 19.8 months, all pts who achieved a ≥CR response had previously manifested Gr2-4 OAEs, while pts who only had Gr0-1 OAEs achieved ≤VGPR. Conclusion: Our analyses highlight the complex association between OAEs and clinical activity, indicating the idiosyncratic nature of a patient's response to belamaf in terms of ocular toxicity and efficacy. Indeed, data reveals that early manifestation of at least moderately severe OAEs (Gr≥2) correspond to early deep responses, a phenomenon observed across all dose levels. Additionally, dose intensity (DI) does not have a linear association with hematologic response, as pts with lower cumulative DI manifested deeper responses. Furthermore, an extended dosing interval due to OAEs is also a hallmark of better efficacy. Conclusively, OAEs may have a predictive and, potentially, also a prognostic role. Moving forward, the association between OAEs and efficacy warrants further investigation in larger sample sizes.

12. REAL-WORLD OUTCOMES OF PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA TREATED WITH TECLISTAMAB AND TALQUETAMAB; A MULTICENTER ANALYSIS FROM THE GREEK MYELOMA STUDY GROUP

Ioannis Ntanasis-Stathopoulos[1], Eirini Katodritou[2], Evdoxia Hatjiharissi[3], Emmanouil Spanoudakis[4], Vasiliki Douka[5], Despina Fotiou[1], Vasiliki Labropoulou[6], Dimitra Dalampira[2], Vasiliki Spiliopoulou[1], Theodosia Papadopoulou[2], Dimitris Christoulas[7], Panagiotis Malandrakis[1], Anthi Bouchla[8], Vasiliki Pappa[8], Efstathios Kastritis[1], Evangelos Terpos[1], Meletios-Athanasios Dimopoulos[1], Maria Gavriatopoulou[1]

[1]Department of Clinical Therapeutics, Alexandra General Hospital, National and Kapodistrian University of Athens, Athens, Greece, [2]Department of Hematology, Theagenio Cancer Hospital, Thessaloniki, Greece, [3]1st Department of Internal Medicine, division of Hematology, AHEPA University Hospital, Thessaloniki, Greece, [4]Department of Haematology, Democritus University of Thrace Medical School, Alexandroupolis, Greece, [5]Hematology Department & HCT Unit G. Papanicolaou Hospital, [6]Hematology Division, Department of Internal Medicine, University of Patras, Medical School, Patras, Greece, [7]251 General Air Force Hospital, [8]Attikon General University Hospital of Athens

OBJECTIVE: To assess the real-world use of the recently approved bispecific antibodies teclistamab (TEC) and talquetamab (TAL) in patients with relapsed/refractory multiple myeloma (RRMM).
METHODS: We retrospectively evaluated the efficacy and safety outcomes of patients with RRMM treated with the approved schedule of TEC or TAL at 8 Greek centers until 30/06/2024.
RESULTS: Thirty-five patients were included; 24 on TEC (median age 66.5 years, 44-85, 45.8% females) and 11 on TAL (57 years, 50-60, 18.2% females). 10 (41.7%) and 1 (9.1%) were primary refractory, whereas 13 (54.2%) and 10 (90.9%) were penta-refractory, respectively. They had received a median of 5 (range 3-11) and 7 (5-11) prior lines of treatment, respectively. After a median of 8 and 7 cycles (3-23 and 2-17), respectively, best responses included 7 (33.4%) CR or better, 3 (12.5%) VGPR and 7 (29.2%) PR for TEC while 1 (9.1%) CR or better, 2 (18.2%) VGPR, 2 (18.2%) PR, 1 (9.1%) MR and 3 (27.3%) SD for TAL. The median time to first response was 36 (20-120) and 42 (15-67) days and the median time to best response was 56.5 (range 20-211) and 56 (15-194) days, respectively. 3/7 patients with EMD on TEC responded (42.9%) and 2/6 on TAL (33.3%). Every patient was hospitalized at least for the initial administration of the drug. Fourteen patients (58.3%) on TEC are still ongoing treatment in remission, 1 (4.2%) is off treatment but in remission, while 5 (20.8%) have discontinued due to PD (5%) and 4 (23.6%) have died (3 due to PD, 1 due to COVID-19); two (8.3%) were lost to follow-up. For TAL, 5 patients (45.5%) are still undergoing treatment on remission, whereas 6 (54.5%) have died due to PD. At a median follow-up of 4.6 months (0.2-13.5) for TEC and 7.8 months (1.1, 19.8) for TAL, the median progression-free survival (PFS) was not reached (NR) and was 6.9 (95% CI: 3.87, NA) months, respectively. Median overall survival (OS) was NR for TEC, while it was 11.5 months (95% CI: 7.8, NA) for TAL. Eight patients (33.3%) on TEC and 8 patients (72.7%) on TAL developed grade 1-5 infections with the first being at a median of 3 (1-15) and 1 (1-5) cycles, respectively. Therapy-induced CRS was documented in 15 (62.5%) TEC and 7 (63.6%) TAL patients. There were 5 (20.8%) and 7 (63.6%) incidences of CRS after dose step-up. The median grade for both groups was 1 (1-3). There was only one case of Immune effector cell-associated neurotoxicity syndrome (ICANS) in the TEC group. There were 10 (41.7%) cases of Hypogammaglobulinemia on TEC. Moreover, there were 7 (29.2%) and 5 (45.5%) cases of grade 3 or 4 neutropenia and 8 (33.3%) and 5 (45.5%) cases of grade 3 or 4 thrombocytopenia, respectively. There were with 3 (12.5%) cases of grade 2 rash and 4 (36.4%) nail changes in TAL and 3 (12.5%) cases of grade 1-3 rash in the TEC group. Conclusion: Real-world outcomes confirm the efficacy and safety profile of TEC and TAL in RRMM, comparable to clinical trials.

13. EVALUATION OF PATIENTS DIAGNOSED WITH ADULT-ONSET LANGERHANS CELL HISTIOCYTOSIS: A SINGLE CENTER EXPERIENCE

Kübra Oral[1], Ayşe Uysal[1]

[1]Firat University School of Medicine Hematology Department

OBJECTIVE: Langerhans cell histiocytosis (LCH) is a rare disease resulting from reactive clonal proliferation of dendritic cells, most commonly affecting bones and skin. It can present with a wide range of clinical manifestations, from unifocal single-system disease to multifocal/multisystem involvement. Due to its rarity and diverse disease spectrum, various treatment approaches are utilized ranging from minimal conservative chemotherapy to intensive combination therapies. The aim of this study is to present our center experiences with this rare disease.

METHODS: Five patients with diagnosed LHH who followed up at the Hematology department of Fırat University between August 2018 and August 2023 was included in this study included. Patient demographics and clinical characteristics, such as age, gender, organ/system involvement, and treatments received were evaluated.

RESULTS: The median age of the patients is 27 (22-38) and 2 (40%) of them are female. Four of them were diagnosed with bone biopsy and 1 with excisional lymph node biopsy. Two patients were smokers and these patients developed pulmonary involvement during their follow-up. The involvement sites were skin, lymph node, thymus and bones. The involvement areas of the patients with bone involvement were in the costa, femur, vertebra and cranial bones. Vinblastine plus prednisolone (VP) was applied to 3 of our patients as initial treatment. Of these 3 patients, 1 patient had a complete response with VP, 1 patient received radiotherapy (RT) due to local recurrence after VP treatment, a complete response was obtained after RT, and 1 patient developed early relapse with skin involvement after VP treatment. Cladribine treatment was applied to this patient who had skin involvement after VP treatment. The patient, who developed an allergic reaction under cladribine treatment, was switched to methotrexate plus 6-mercaptopurine treatment, and this treatment still continues. Cytosine arabinoside (ARA-C) was applied as initial treatment to 2 of our patients. One of these patients continues with the 9th cycle of ARA-C treatment as a complete response to the current treatment. In other patient, who received ARA-C as initial treatment, RT was given due to local progression in the vertebral bones after the 9th cycle of ARA-C. This patient, whose pulmonary involvement progressed during follow-up, was treated with 4 cycles of cladribine. As there was progress under cladribine treatment, vemurafenib treatment was applied and the pulmonary symptoms regressed with vemurafenib treatment. Vemurafenib treatment still continues.

CONCLUSION: While surgery, RT and prednisolone are recommended for unifocal involvement, VP, cladribine, ARA-C, methotrexate a single agent or in combination are recommended therapy for multifocal/multisystem involvement. In our study, VP and ARA-C treatments were used as the first step in multifocal/multisystem involvement. Cladribine, methotrexate combination treatment and vemurafenib was used in patients who developed relapse or progression. As a result, since LHH in adulthood is rare and has no standard treatment, case-based treatment options should be determined in line with expert opinions.

14. SUCCESSFUL TREATMENT OF A PATIENT WITH SYNCHRONOUS LUNG ADENOCARCINOMA AND ACUTE MYELOID LEUKEMIA BY A COMBINATION OF VENETOCLAX WITH AZACITIDINE

Emel İşleyen Kaya[1], Simten Dağdaş[1], Fahir Öztürk[1], Merve Ecem Yön Erdoğan[1], Mehmet Sezgin Pepeler[1], Bülent Yalçın[1], Aynur Albayrak[1], Funda Ceran[1], Gülsüm Özet[1]

[1]Ankara Bilkent City Hospital

OBJECTIVE: Synchronous acute myeloid leukema and lung adenocarcinoma coexistence is very rare in the literatüre. It's prognosis is poor and because of no standard approach has been defined treatment and follow-up should be individualized. We wanted to point out that remission, which could not be achieved after classical 3+7 induction chemotherapy, was achieved after venetoclax +azacitidine (VNT + AZA) treatment in a 58-year-old female patient with synchronous coexistence of solid tumor and hematological malignancy. In addition, our case in which lung cancer metastasis was detected in the bone marrow after AML remission is also important as it sets an example because there is no similar case in the literature before.

METHODS: A 58-year-old female patient was evaluated by pulmonologists with complaints of stinging and pain in the chest while breathing. In the PET CT scan of the patient; A few lymph nodes with increased F-18 FDG uptake. The lymph node biopsy was reported as adenocarcinoma metastasis. The patient was consulted to us due to anemia and thrombocytopenia Laboratory tests revealed a hemoglobin level of 9 g/dl, thrombocytopenia (27 x10^9/L), and leukocytosis (18.70 x10^9/L). The bone marrow biopsy was reported as diffuse blastic cell infiltration compatible with AML 1-2. Any specific mutation was detected. Oncology recommended that AML treatment should be given primarily to the patient because she not suitable for systemic chemotherapy due to cytopenia in her current condition On the 28th day of 3+7 induction chemotherapy (cytarabine 200 mg/day continuous infusion on days 1-7, daunorubicin 45 mg/m2/day on days 1-3) bone marrow examination showed blastic cell infiltration was continue. After induction chemotherapy, immune thrombocytopenia and intracranial bleeding developed. Because of these comorbidities anthracycline chemotherapy could not be given and intermediate dose ARA-C (1.5 g/m2, 1-3 days) was given. As the blastic infiltration persisted on the follow-up bone marrow biopsy, it was planned to switch to azacitidine + venetoclax treatment

RESULTS: The patient's bone marrow was in remission after 1 cycle of azacitidine (7 days, 75 mg/m^2)+Venetoclax (28 days, 100 mg/day) and after two course bone marrow compatible with epithelial lung carcinoma metastasis. The patient, was found to be anaplastic lymphoma kinase (ALK) positive and compatible with lung carcinoma metastasis, was referred to medical oncology to be evaluated for oncological treatment. The oncologist started the patient Brigatinib. Following remission of lung cancer, azacitidine + venetoclax treatment was planned to be continued. Conclusion: In our case, AML treatment was first arranged due to profound cytopenia, and after treatment, bone marrow hematological complete response was reported as compatible with epithelial tumor metastasis. There are rare cases of synchronous AML and lung adenocarcinoma in the literature. However, we could not find any case of lung cancer metastasis to bone marrow after remission was achieved after AML treatment. Our case is the first in this regard. It is known that azacitidine and venetoclax treatment are effective in the treatment of AML. However, it is also important as it is the first literature data showing that it is effective in the synchronous coexistence of solid tumor and AML.

15. ELEVATED EXPRESSION LEVELS OF ADRENOMEDULLIN TREND WITH SUBOPTIMAL TREATMENT RESPONSE AND INFERIOR SURVIVAL OF NDMM PATIENTS

Angelos Giannakoulas[1], Panagiotis Stoikos[1], Evangelia Kouvata[1], Katerina M. Kontouli[2], Georgios Fotiadis[1], Georgia Stefani[1], Athanasios Antoniou[1], Konstantinos Leontopoulos[1], Grigorios D. Amoutzias[3], George Vassilopoulos[1], Nikolaos Giannakoulas[1]

[1]Hematology Department, University Hospital of Larissa, [2]Laboratory of Hygiene and Epidemiology, University of Thessaly, [3]Bioinformatics Laboratory, Department of Biochemistry & Biotechnology, University of Thessaly

OBJECTIVE: Adrenomedullin (AM) is a multifunctional peptide which mainly regulates vasodilation and maintains vascular integrity but is also implicated in the pathogenesis of several malignancies, including multiple myeloma (MM). It has been shown that adrenomedullin enhances MM-driven angiogenesis. However, the clinical impact of AM remains unknown.

METHODS: We evaluated the expression of adrenomedullin in 32 newly diagnosed multiple myeloma (NDMM) patients and 20 age and sex-matched healthy donors. Diagnosis of MM was based on IMWG consensus criteria. Patients received either VCD or VRD based regiments. Response was evaluated after five cycles of induction therapy. All samples were taken at the time of diagnosis. Bone marrow aspirates were collected in EDTA-containing tubes. Bone marrow mononuclear cells (BMMNCs) were separated using density gradient separation with Ficoll, total RNA was extracted from BMMNCs and then RNA was reverse transcribed into cDNA. RT q-PCR was carried out with CYBR green 1 as fluorescence dye. ACTB was used as housekeeping gene. Gene expression levels were analyzed with the Livak method.

RESULTS: To establish the differential expression of AM in MM, we first compared AM levels of the ADM gene between NDMM patients and healthy donors. AM mRNA abundance was 10-fold higher in the NDMM group compared to the HD group ($P < 0.0001$). We, then, categorized patients into two groups based on the expression levels of AM. The median DCT value of the NDMM population served as cut-off point. The first group (High) comprised of patients with elevated expression measures of AM (n=16, median DCT 4.6, range 2.7-5.8) and the second one (Low) comprised of patients with lower measures (n=16, median DCT 7.8, range 6.1-10.3). The 2 groups did not differ in age, sex, percentage of bone marrow infiltration, ISS stage, R2-ISS stage and were equally treated with VRD-based or VCD-based regiments. The Overall response rate (≥ PR) was 56% (n = 9/16) for the high group and 81% (n = 13/16) for the low group. After a median follow up period of 23 months (range 1-57 months), 14 (87%) and 8 (50%) patients from the high and low expression group, respectively, have relapsed or died with a median time to progression or death of 16 (range 1-42) and 16.5 (range 1-55) months respectively. Kaplan-Meier curves were used to calculate probability of survival. The median estimated overall survival for patients with elevated AM measures was 29.5 months compared to 55 months for patients with lower AM measures (HR = 2.1, 95% CI of ratio 0.7-6.1, P = 0.1). In univariate analysis, age (HR = 1.6, P = 0.02), LDH (HR = 1.01, P = 0.002) and b2-microglobulin (HR = 1.15, P = 0.03) were independent factors predicting poor survival whereas elevated levels of AM increased the risk of the event (for every DCT reduction by one unit; HR = 1.2, P = 0.1). In multivariant analysis, age and R2-ISS stage 4 were the only significant predictive factors for survival. Conclusion: Our findings indicate that elevated levels of AM trend with suboptimal treatment response and inferior survival of NDMM patients.

16. A COMPREHENSIVE IMAGING ANALYSIS OF BONE DISEASE BURDEN IN 119 PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA

Nikolaos Kanellias[1], Evangelos Terpos[1], Vassilis Koutoulidis[2], Ioannis Ntanasis-Stathopoulos[1], Stylianos Mavropoulos-Papoudas[2], Maria Douka[2], Maria Gavriatopoulou[1], Panagiotis Malandrakis[1], Vasiliki Spiliopoulou[1], Foteini Theodorakakou[1], Despina Fotiou[1], Magdalini Migkou[1], Evangelos Eleutherakis-Papaiakovou[1], Efstathios Kastritis[1], Lia-Angela Moulopoulos[2], Meletios-Athanasios Dimopoulos[1]

[1]Department of Clinical Therapeutics, Alexandra General Hospital, National and Kapodistrian University of Athens, Athens, Gree, [2]1st Department of Radiology, School of Medicine, Aretaieion Hospital, National and Kapodistrian University of Athens, Athens, Greece

OBJECTIVE: To evaluate the bone disease burden in patients with newly diagnosed MM using whole body low dose computed tomography (WBLDCT) and explore possible correlations with survival outcomes.
METHODS: We consecutively enrolled patients with NDMM who were WBLDCT assessed at a single referral center according to standard clinical practice.
RESULTS: 119 patients (57.5% females) were included, with a median age of 67 years (range 37-81). Patients were assessed per ISS and R-ISS stage as follows: 31 (26.3%) and 20 (16.9%) stage 1, 30 (25.4%) and 71 (60.2%) stage 2, 57 (48.3%) and 27 (22.9) stage 3, respectively. As per R2-ISS they were distributed as follows: 48 (40.7%) low risk, 24 (20.3%) low-intermediate risk, 33 (28.0%) intermediate-high risk and 13 (11.0%) high risk. 73 patients (61.3%) had performance status 0-1, whereas 19 (16.1%) had at least one high-risk cytogenetic abnormality. The patients received induction treatment as follows: 80 (67%) based on proteasome inhibitors, 14 (12%) based on immunomodulatory drugs, 22 (19%) based on both a PI and an IMiD and 3 (2%) based on anti-CD38 monoclonal antibodies. 31 (26.3%) of the patients underwent autologous stem-cell transplantation. During a median follow-up of 4.2 years (range 0.1-5.4), 79 patients (67.0%) showed disease progression and 63 (54.2%) died. The median progression-free survival (PFS) was 2.19 years (95% CI: 1.61-3.31) and median overall survival (OS) was 6.24 years (95% CI: 4.06-not reached). Regarding osteolysis assessment, the median (range) number of osteolyses in each bone group were as follows: 2 (0-96) for the spine (cervical spine, thoracic spine, lumbar spine, sacrum), 0 (0-30) for the skull, 0 (0-41) for the shoulder (left and right clavicles, left and right scapulae), 0 (0-28) for the appendices (left and right femurs, left and right humerus) and 0 (0-42) for the ribs (right and left ribs). Regarding the ASMC assessment in the bilateral femurs and humerus, 47 patients (39.5%) showed fatty ASMCs, 39 patients (32.8%) had diffuse ASMCs, 30 patients (25.2%) had nodular ASMCs, whereas 38 patients (31.9%) had mixed ASMCs subtypes. The 119 patients were stratified according to the presence (n=52) or absence (n=67) of VCFs. When applying the presence or not of VCFs as a single predictor for PFS and OS, the results were significantly worse survival if at least one VCF was present. Specifically, median PFS was 42.7 months for patients without VCFs compared to 19.8 months for patients with at least one (HR 1.69, 95%CI: 1.09 – 2.62, P = 0.02). Similarly, median OS was prolonged in patients without VCFs compared to those with at least one (HR 1.99, 95%CI: 1.21-3.25, P = 0.006). However, among all the examined imaging variables, no factor or combination factors had independent significance for patient prognosis.
CONCLUSION: Although the presence of VCFs at WBCT at diagnosis of MM was correlated with survival outcomes in the univariate analysis, none of the imaging parameters retained statistical significance in the multivariate analysis. Therefore, it seems that the extend of the MBD burden at diagnosis does not impact OS in the era of modern anti-myeloma treatment regimens.

17. CLINICAL CHARACTERISTICS AND OUTCOME OF EARLY-STAGE DIFFUSE LARGE B CELL LYMPHOMA OF FEMALE GENITAL TRACT: A RETROSPECTIVE STUDY OF THE HELLENIC COOPERATIVE LYMPHOMA GROUP

Evgenia Verrou[1], Sotirios G Papageorgiou[2], Maria Bouzani[3], Aggeliki Sevastoudi[1], Theodora Triantafyllou[1], Aikaterini Daiou[1], Dimitra Dalampira[1], Maria Arapaki[4], Chara Giatra[3], Anastasia Banti[5], Gerasimos Kyriakidis[6], Dionisios Stoumpos[7], Nikolaos Karampatzakis[1], Theodosia Papadopoulou[1], Anastasios Radounislis[1], Maria Kotsopoulou[7], Anastasia Pouli[6], Evdokia Mandala[8], Vassiliki Pappa[2], Emmanouil Spanoudakis[9], Theodoros P. Vassilakopoulos[4], Eirini Katodritou[1]

[1]Department of Hematology, Theagenion Cancer Hospital, Thessaloniki, Greece, [2]Second Department of Internal Medicine, Hematology Unit, Attikon Hospital, National and Kapodistrian University of Athens, Athens, Greece, [3]Department of Hematology and Lymphoma, Evangelismos General Hospital, Athens, Greece, [4]Department of Hematology and Bone Marrow Transplantation, Laikon General Hospital, National and Kapodistrian University of Athens, Athens, Greece, [5]Department of Hematology, Papageorgiou Hospital, Thessaloniki, Greece, [6]Department of Hematology, Aghios Savvas Cancer Hospital, Athens, Greece, [7]Department of Hematology, Metaxa Cancer Hospital, Piraeus, Greece, [8]4th Department of Internal Medicine, Hippokration General Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece, [9]Department of Hematology, Democritus University of Thrace, Alexandroupolis, Greece

OBJECTIVE: Involvement of Female Genital Tract (FGT) by Diffuse Large B Cell Lymphoma (DLBCL) represents a rare diagnosis. Especially data regarding early-stage disease is limited. Previous studies showed controversial results about the risk of Central Nervous System (CNS) relapse in this entity. Herein, we describe one of the largest reported real-world series of patients with early-stage FGT DLBCL aiming to investigate the clinicopathological characteristics, response to therapy and survival outcomes in the immunochemotherapy era.

METHODS: We collected retrospectively, data of patients from nine Hematology Departments in Greece from 2002 until 2022. The pathological diagnosis of DLBCL was based on the World Health Organization classification (WHO). DLBCL Cell of Origin (COO) subtype was classified according to the immunochemistry-based algorithm developed by Hans et al. Bone marrow biopsy and Computed tomography (CT) or Positron Emission Tomography (PET)-CT were used for baseline staging. Early-stage was defined as biopsy proven DLBCL truly localized to the uterus or ovary or demonstrating only localized lymphadenopathy, i.e. stage IE and IIE according to the Ann Arbor staging system. Recorded data included, age at diagnosis, disease localization, Revised International Prognostic Index (R-IPI), serum lactate dehydrogenase (LDH), beta-2 microglobulin (β2M), Germinal Center B-cell (GCB) or non-GCB COO, treatment, response and outcomes. Overall Survival (OS), Lymphoma Specific Survival (LSS) and Freedom from Progression (FFP) were plotted by the Kaplan-Meier method. Age, LDH, β2M, Ann-Arbor stage, R-IPI, disease localization and COO subtype were examined as possible prognostic factors for OS and LSS, using a univariate cox regression analysis.

RESULTS: We analyzed 21 consecutive patients with biopsy proven DLBCL from uterus or ovary classified as stage IE or IIE out of 1905 newly diagnosed DLBCL patients (1.1%). Diagnosis was documented by excision surgery in seven patients. Uterine and ovarian localization was observed in 14 and 7 patients, respectively. Median age was 66 years (range 33-96); 9/21 (43%) were < 55 years. Regarding Cell of Origin DLBCL subtype, Germinal Center B-cell (GCB) subtype was found in 7 patients, non-GCB in ten and non-classified in 4 patients. Regarding therapy 19/21 patients received rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (RCHOP) (median number of cycles: 6, range: 3-6), and one patient received R-miniCHOP. One patient with stage I ovarian involvement refused any further treatment after total hysterectomy. Three patients received radiotherapy (RT) complementary to RCHOP. Four patients received CNS prophylaxis. Response evaluation was available in 20 patients and all achieved Complete Response (CR). After a median follow up of 57 months (95% CI: 51-63), 5 patients deceased (lymphoma relapse: 2, breast cancer: 1, covid-19 infection: 1, therapy-related toxicity: 1) and 16/20 patients (80%) remained alive in CR. OS, LSS and FFP were 78%, 89% and 90%, respectively. There was no correlation of patients' characteristics with survival parameters. Interestingly, none of the patients in our study developed secondary CNS involvement.

CONCLUSION: Our results indicate that localized FGT DLBCL exhibits a good prognosis and may not increase the risk for secondary CNS involvement. These results are of importance considering the rarity of the disease and the difficulty to conduct prospective studies.

18. AUTOLOGOUS TRANSPLANTATION IS THE STRONGEST PROGNOSTIC FACTOR FOR OVERALL SURVIVAL IN MULTIPLE MYELOMA PATIENTS WITH DELETION 17P: 20-YEAR REAL-WORLD EXPERIENCE OF THE GREEK MYELOMA STUDY GROUP

Eirini Katodritou[1], Efstathios Kastritis[2], Dimitra Dalampira[1], Emmanouil Spanoudakis[3], Anastasia Pouli[4], Sosana Delimpasi[5], Aggeliki Sevastoudi[1], Ioannis Ntanasis-Stathopoulos[2], Fotini Theodorakakou[2], Theodora Triantafyllou[1], Despina Fotiou[2], Aikaterini Daiou[1], Prodromos Koutoukoglou[1], Kyriaki Tsirou[1], Gerasimos Kyriakidis[4], Nikos Kanellias[2], Magdalini Migkou[6], Theodosia Papadopoulou[1], Ioannis Kostopoulos[7], Marie-Christine Kyrtsonis[8], Maria Kotsopoulou[9], Maria Gavriatopoulou[2], Evgenia Verrou[1], Meletios-Athanasios Dimopoulos[2], Evangelos Terpos[2]

[1]Department of Hematology, Theagenio Cancer Hospital, Thessaloniki, Greece, [2]Department of Clinical Therapeutics, National and Kapodistrian University of Athens, Athens, Greece, [3]Department of Hematology, University Hospital of Alexandroupolis, Alexandroupolis, Greece, [4]Department of Hematology, Agios Savvas Cancer Hospital, Athens, Greece, [5]Department of Hematology and Bone Marrow Transplantation Unit, Evangelismos Hospital, Athens, Greece, [6]Department of Clinical Therapeutics, National and Kapodistrian University of Athens, Athens, Greeceogy, National and Kapodistrian University of Athens, Athens, Greece, [7]Department of Biology, National and Kapodistrian University of Athens, Athens, Greece, [8]First Department of Propaedeutic Internal Medicine, Laikon General Hospital, National and Kapodistrian University of Athens, Athens, Greece, [9]Department of Hematology, Metaxa Cancer Hospital, Piraeus, Greece

OBJECTIVE: Deletion 17p (del17p) is a strong negative prognostic factor for survival in Multiple Myeloma (MM), and it is included in both the revised international staging system (RISS) and its 2nd revision (R2-ISS). Our aim was to compare characteristics and outcomes of MM patients with or without del17p, and to explore possible other adverse prognostic factors for overall survival (OS) in patients with del17p, in the real-world setting.

METHODS: We analyzed 1337 MM patients (M/F: 665/672, median age: 66, range: 33-92, IgG: 786, IgA: 350, light chain: 177, IgD: 8, non-secretory: 14, IgM: 2) who were diagnosed from 2003-2023, and included in the Greek Myeloma Study Group registry. Of those, 129 (9.6%) patients had del17p (median age: 65, range: 38-85; M/F: 67/62); 74/129 (57.4%) had del17p as a single abnormality (del17p-s), whereas 55 (42.6%) had del17p plus ≥1 other high-risk abnormality (del17p-plus). Results: Age, eGFR, calcium, albumin, platelet counts, and bone marrow infiltration did not differ between del17p vs others (control group); LDH and β2-microglobulin were higher, while hemoglobin was lower in del17p patients ($p<0.05$). Expectedly, R-ISS3 and R2-ISS4 were more common in patients with del 17p (31 vs 9% and 41% vs 26%, respectively; $p<0.001$). All patients were treated with novel anti-myeloma combinations; 487 (36.5%) received lenalidomide-based triplets (LBT i.e. lenalidomide-proteasome inhibitor-dexamethasone) or daratumumab-based regimens (DBR). Regarding del17p patients, 41/129 (32%) received LBT/DBR and 40 (31%) underwent autologous transplantation (ASCT) upfront; induction therapy did not differ between groups. After a median follow up of 57 months (95% CI: 53-61), 80/129 (62.0%) patients with del17p vs 479/1208 (39.6%) of controls deceased ($p<0.001$). Median PFS and OS of patients with del17p vs others was 19 (95% CI: 15-23) vs 34 months (95% CI: 31-37), and 36.8 (95% CI: 26-47.6) vs 83 months (95% CI: 75-91), respectively ($p<0.001$). PFS and OS did not differ between del17p-s vs del17p-plus patients. In the multivariate analysis for the whole population del17p, eGFR<40mL/min/1.73m2, R2-ISS, LBT/DBR induction and ASCT were significant prognosticators for OS. High-risk abnormalities other than del17p had no impact on OS. In multivariate analysis for the de17p cohort, ASCT was the only independent prognostic factor for OS ($p<0.001$; HzR: 0.26 95% CI: 0.18-0.40). Median OS for patients who underwent ASCT vs others was 52.3 (95% CI: 25.9-78.7) vs 30 months (95% CI: 24.6-35.3), respectively ($p=0.003$).

CONCLUSION: We conclude that, in the real-world setting, del17p remains an independent prognostic factor for OS, surpassing the predictive value of other high-risk abnormalities. For patients with del17p, neither baseline prognostic markers/staging systems or current upfront regimens predicted for OS; ASCT remains a strong prognosticator underscoring its established therapeutic value in this high-risk population.

19. LEPTOSPIROSIS PRESENTING WITH MULTIPLE ORGAN FAILURE: A DIAGNOSTIC CHALLENGE

Sukriye Miray Kilincer Bozgul[1], Ilkce Akgun Kurtulmus[2], Devrim Bozkurt[1]

[1]Ege University Faculty of Medicine, Department of Internal Medicine, Division of Intensive Care, [2]Torbalı State Hospital

OBJECTIVE: Leptospirosis is a zoonotic infection caused by spirochetes of the genus Leptospira. While 90% of the patients have non-icteric asymptomatic form, approximately 5-10% develop multiple organ failure and mortality is high. Leptospirosis is rarely suspected due to the non-specific clinical presentation. Here we report an uncommon case of multiple organ failure caused by leptospirosis in a 67-year old man who was succesfully treated with antibiotics and intravenous immunoglobulins (IVIG).

METHODS: A 67-year-old male presented to the hospital with a history of nausea, vomiting and abdominal pain. He also had a history of decrease in urine output and darkening in urine colour for two days. He had no significant medical history. On hospital admission, the patient was conscious with a blood pressure of 120/75 mm/Hg, heart rate of 118/min, body temperature of 37,5° C, respiratory rate of 18/min, oxygen saturation of 98% on ambient air. Respiratory sounds revealed crepitant ral and he had pretibial edema. Due to acute renal failure, thrombocytopenia and high acute phase reactant findings in laboratory results, the patient was hospitalised in the internal medicine intensive care unit with a prediagnosis of sepsis and multiple organ failure. Laboratory findings at admission and follow-up are shown in Table-1. During follow-up, the day after admission; with worsening of consciousness and hypotension, the patient developed septic shock. Progression was also observed in laboratory results (Table 1). He was treated with wide spectrum antibiotics, positive inotropic agents and renal replacement therapy as a result of worsening renal functions and anuria. There was no positive blood and urine cultures. Viral markers were negative. Leptospira, rickettsia and coxiella serologies were also investigated because of fever, renal failure, jaundice and severe thrombocytopenia. Leptospira interrogans PCR resulted positive. Doxycycline and IVIG were added to the treatment. Clinical and laboratory response was obtained on the 3rd day after treatment. At the end of 8 days, the acute kidney injury resolved, clinical and laboratory parameters improved and he had complete recovery on the 15th day. After recovery, he mentioned a history of contact with a stray dog and there was no other significant history.

RESULTS: We describe a rare and unusual presentation of leptospirosis. Zoonoses are rarely involved in sepsis and multiple organ failure and leptospirosis is often not included in the differential diagnosis due to it's asymptomatic course. In our country, mortality has been reported to reach 10-17% in severe cases.

CONCLUSION: It is important to keep in mind that initial presentation of leptospirosis could be as multiple organ failure.

20. RISK OF PROGRESSION FROM SMOLDERING TO SYMPTOMATIC MYELOMA IN THE ERA OF CRAB/SLIM CRITERIA

Efstathios Kastritis[1], Panagiotis Malandrakis[1], Irene Solia[1], Ioannis Ntanasis-Stathopoulos[1], Foteini Theodorakakou[1], Vasiliki Spiliopoulou[1], Despina Fotiou[1], Magdalini Migkou[1], Nikolaos Kanellias[1], Maria Roussou[1], Evangelos Eleutherakis-Papaiakovou[1], Christine-Ivy Liacos[1], Nefeli Mavrianou Koutsoukou[1], Katerina Chrisostomidou[1], Maria Gavriatopoulou[1], Evangelos Terpos[1], Meletios-Athanasios Dimopoulos[1]

[1]Department of Clinical Therapeutics, Alexandra General Hospital, National and Kapodistrian University of Athens, Athens, Greece

OBJECTIVE: This study aims to describe risk and patterns of progression among patients with smoldering multiple myeloma (SMM), diagnosed after 2014.

METHODS: The analysis included 427 SMM patients diagnosed and followed in the Department of Clinical Therapeutics, Athens, between 2014 and 2023, according to the contemporary practices, that include advanced imaging at the time of diagnosis and during follow up. During the same period 486 patients were diagnosed with non-IgM monoclonal gammopathy of undetermined significance (MGUS). Results: The median age of the 427 SMM patients was 65 years (vs 67 for MGUS); according to 20-2-20, 50% of were low risk, 31% intermediate and 19% high. According to IMWG scoring tool, 63% were low, 31% low-intermediate, 5% intermediate and <1% high risk. The median follow-up was 36 months (IQR 17-64). Fourty-two SMM patients (10.1%) progressed to symptomatic MM (vs 6 (1.2%) in MGUS). The 1-, 2- and 3- year cumulative progression rate was 4%, 9% and 13%, respectively. For MGUS patients the cumulative 1-, 2- and 3-year progression rate was 1%, 2% and 2%, respectively. Per IMWG's 20-2-20, the 1-, 2- and 3-year progression rate was 0%, 1% and 2% for low risk and was 2%, 3.5% and 6% for intermediate risk SMM; thus, the 1-, 2- and 3- years progression risk among low and intermediate risk SMM was 1%, 2% and 3%. However, among high risk SMM, the 1-, 2- and 3-year progression rate was 18%, 28% and 43% ($p<0.001$). According to the IMWG scoring tool, 3-year progression was 0% for low risk, for low-intermediate the 1-, 2- and 3-year progression rate was 6%, 15% and 24%, and for intermediate and high 33%, 53% and 66%. Among SMM patients that progressed to symptomatic MM, one (2.5%) progressed by developing a soft tissue plasmacytoma, one (2.5%) with acute renal dysfunction, 13 (31%) with anemia, 14 (33%) with lytic bone disease (BD) and 13 (31%) based on SLiM criteria. Among patients with BD, lytic lesions were detected mostly during follow up imaging, and only in one patient were associated with symptoms (fracture). Among patients with MGUS, progression events included lytic BD detected during routine imaging in 2, acute renal dysfunction in 2 and SLiM criteria in 2.

CONCLUSION: In SMM patients diagnosed by 2014 IMWG criteria and followed with contemporary imaging, progressoin events mostly included anemia, SLiM criteria or asymptomatic BD. The risk of imminent progression among those with low or intermediate risk per 20-2-20 or low risk per IMWG is low and is similar to that of MGUS. Among those at high risk per 20-2-20, the progression risk seems to be lower than in original cohorts, probably due to advanced imaging at diagnosis. The IMWG tool may be more accurate but identifies fewer intermediate/high-risk individuals. Careful assessment of patients with SMM at the time of diagnosis, with the use of advanced imaging to ensure those at low/intermediate risk about their prognosis, is essential. For high-risk patients, clinical trials should be considered, but overtreating should be avoided based only on current prognostic tools.

21. EARLY DETECTION OF PROGRESSION WITH SEQUENTIAL WHOLE BODY LOW DOSE CT IN PATIENTS WITH SMOLDERING MULTIPLE MYELOMA

Magdalini Migkou[1], Vassilis Koutoulidis[2], Ioannis Ntanasis-Stathopoulos[1], Panagiotis Malandrakis[1], Vasiliki Spiliopoulou[1], Charalampos Filippatos[1], Despina Fotiou[1], Nikolaos Kanellias[1], Evangelos Eleutherakis-Papaiakovou[1], Efstathios Kastritis[1], Evangelos Terpos[1], Meletios-Athanasios Dimopoulos[1], Lia-Angela Moulopoulos[2], Maria Gavriatopoulou[1]

[1]Department of Clinical Therapeutics, Alexandra General Hospital, National and Kapodistrian University of Athens, Athens, Greece, [2]1st Department of Radiology, School of Medicine, Aretaieion Hospital, National and Kapodistrian University of Athens, Athens, Greece

OBJECTIVE: Whole-body low-dose CT (WBLDCT) is recognized as the gold standard for detecting myeloma bone disease (MBD) and is now part of the surveillance protocol for patients with smoldering multiple myeloma (sMM). In this study, we assessed the role of sequential WBLDCT evaluations in the early detection of patients progressing to symptomatic disease.

METHODS: Patients diagnosed with SMM according to the 2003 IMWG definition were consecutively evaluated using WBLDCT. Assessments were conducted at baseline, one year after diagnosis, and annually thereafter.

RESULTS: We prospectively evaluated 113 patients with SMM, with a median age at diagnosis of 60 years (ranging from 35 to 85 years), and 53.1% of the participants were female. The median number of WBLDCT exams performed per patient was 3 (ranging from 1 to 6). According to the IMWG 2/20/20 risk stratification model, the distribution of patients was 36.3% low risk, 33.6% low-intermediate risk, 24.0% intermediate risk, and 4.4% high risk. Over a median follow-up period of 8.81 years (IQR 7.3–10.7 years), 41 patients (36.3%) progressed according to the CRAB-SLiM criteria. Notably, 11 out of these 41 patients (26.8%) progressed exclusively with bone lesions only. The median follow-up period was 8.82 years for bone-only progressors compared to 10.05 years for other progressors. Within this subgroup, 45.5% were at the intermediate-risk stage, 9.1% at the high-risk stage, and only 9.1% at the low-risk stage. The median time to progression (TTP) from asymptomatic to symptomatic disease for all 113 patients was 14.8 years (95% CI: 10.0, NA). For those who actually progressed, the median TTP was 2.95 years (95% CI: 2.46, 4.39). In the subgroup of patients who progressed with bone lesions only, the median TTP was 2.59 years (95% CI: 1.96, NA), compared to 3.02 years (95% CI: 1.96, NA) for other progressors (p=0.244). At the time of progression to symptomatic disease, bone marrow infiltration had significantly increased compared to baseline for bone-only progressors (25.5% versus 44.4%, p = 0.028). There were no differences in ISS and R-ISS distributions between the two subgroups. All patients began antimyeloma treatment immediately after diagnosis of symptomatic disease. 19 patients experienced disease progression at first-line treatment: 3 (27.3%) from the bone-only subgroup and 16 (53.3%) from the others. The median progression-free survival (PFS) for the 41 patients with symptomatic MM was 6.66 years (2.66, NA). For bone-only progressors, the median PFS was not reached and it was 3.43 years (2.10, NA) for the other progressors from sMM to MM (p=0.113). Overall, there were three deaths: 2 among the patients who progressed to MM (1 MM-related) and 1 among the non-progressors. None of the patients who died had progressed with isolated bone involvement.

CONCLUSION: Sequential imaging assessment with annual WBLDCT in patients with sMM enabled early diagnosis of MBD in approximately 10%. Early detection of myeloma progression and prompt initiation of anti-myeloma treatment may prevent end organ damage and improve patient outcomes.

22. CHARACTERISTICS, OUTCOME, AND PROGNOSTIC FACTORS FOR SURVIVAL AND PROGRESSION TO MULTIPLE MYELOMA OF SOLITARY PLASMACYTOMAS: A 30-YEAR EXPERIENCE OF THE GREEK MYELOMA STUDY GROUP

Eirini Katodritou[1], Efstathios Kastritis[2], Dimitra Dalampira[1], Nikos Kanellias[2], Vasiliki Labropoulou[3], Gerasimos Kyriakidis[4], Vasiliki Douka[5], Sosana Delimpasi[6], Dionysios Stoumpos[7], Emmanouil Spanoudakis[8], Sotirios Papageorgiou[9], Despina Fotiou[2], Annita-Ioanna Gkioka[10], Theodora Triantafyllou[1], Ioannis Ntanasis-Stathopoulos[2], Aggeliki Sevastoudi[1], Aikaterini Daiou[1], Foteini Theodorakakou[2], Nikolaos Giannakoulas[11], Chrysavgi Lalayianni[5], Anastasia Pouli[4], Evgenia Verrou[1], Maria Gavriatopoulou[2], Evangelos Terpos[2], Meletios-Athanasios Dimopoulos[2]

[1]Department of Hematology, Theagenio Cancer Hospital, Thessaloniki, Greece, [2]Department of Clinical Therapeutics, National and Kapodistrian University of Athens, Athens, Greece, [3]Department of Internal Medicine, Division of Hematology, University of Patras Medical School, Patras, Greece, [4]Department of Hematology, Agios Savvas Cancer Hospital, Athens, Greece, [5]Department of Hematology and Bone Marrow Transplantation Unit, Papanikolaou General Hospital, Thessaloniki, Greece, [6]Department of Hematology and Bone Marrow Transplantation Unit Evangelismos Hospital, Athens, Greece, [7]Department of Haematology, Metaxa Cancer Hospital, Piraeus, Greece, [8]Department of Hematology, University Hospital of Alexandroupolis, Alexandroupolis, Greece, [9]Department of Hematology, Attikon General Hospital, Athenks, Greece, [10]First Department of Propaedeutic Internal Medicine, Laikon General Hospital, National and Kapodistrian University of Athens, Athens, Greece, [11]Department of Hematology, University of Thessaly, Larissa, Greece

OBJECTIVE: Solitary plasmacytoma (SP) is characterized by the presence of bone or extraosseous tumors composed of malignant plasma cells without evidence of systemic Multiple Myeloma (MM). Radiotherapy (RT) +/- surgical excision (SE) is the standard treatment, while systemic therapy (ST) has not been proven beneficial. We aimed to examine outcomes and prognostic factors for survival and progression to MM in a large cohort of SP patients diagnosed over 30 years and assess the impact of various therapies.

METHODS: We analyzed 172 patients [M/F: 84/88, median age: 62 (17-85), Solitary Bone Plasmacytoma (SBP)/ Solitary Extramedullary Plasmacytoma (SEP): 115/57]. Prognostic factors for overall survival (OS), progression-free survival (PFS), and MM-free survival (MMFS) were determined by cox regression.

RESULTS: Patients' characteristics were similar between SBP and SEP patients; M-protein was more common in SBP patients (67% vs. 37%; p<0.001). Median size of plasmacytomas was larger in SBP vs. SEP pts (5.7 cm vs. 4 cm; p<0.05); SEP was most frequently located in the upper respiratory tract (63%); SBP was more often found in the vertebrae (44%). Therapies included: RT (n=78), RT + ST (n=38), RT+ SE (n=13), ST (n=17), SE (n=12), ST+ SE (n=4), RT+SE+ST (n=10). Median RT dose was 40 cGy (20-60 cGy). Among patients treated with ST, 71% received novel-agent combinations. Overall and complete response (CR) were 94% and 53% respectively, similar between SBP and SEP; 70 patients relapsed with most (77%) experiencing progression to MM +/- new plasmacytomas. After a median follow up of 114 months (95% CI: 79-149), 109 patients were alive, 54 had died (MM progression: 21) and 12 were lost to follow-up. Median OS, 5- and 10-year OS were 224 months, 85% and 69% respectively, similar in both groups; median PFS, and 5- and 10-year PFS were 72 months, 54% and 40% respectively. Median PFS was longer in SEP vs. SBP (132 vs. 63 months; p=0.09). Median MMFS was 121 months for SBP vs. not reached for SEP (p=0.09); 5- and 10-year MMFS for SBP vs. SEP was 65% vs. 75% and 52% vs. 66%, respectively. Age >60 and progression to MM were negative predictors for OS with age >60 maintaining its' significance in the multivariate analysis (HR:3.1; p<0.001); CR was the only significant positive predictor for PFS (HR: 0.51; 0.003). An abnormal baseline free light chain ratio (FLCR) was a negative predictor for progression to MM (HR: 3.5; p=0.03); RT +/- SE significantly reduced the risk for progression to MM (HR: 0.25; p=0.02).

22. CHARACTERISTICS, OUTCOME, AND PROGNOSTIC FACTORS FOR SURVIVAL AND PROGRESSION TO MULTIPLE MYELOMA OF SOLITARY PLASMACYTOMAS: A 30-YEAR EXPERIENCE OF THE GREEK MYELOMA STUDY GROUP

CONCLUSION: Our study, one of the largest multicenter studies on patients with SP, with the longest reported median follow-up to date showed that, patients with SP experience prolonged OS which strongly correlates with patients' age; CR was a stronger predictor of PFS than the type of SP. An abnormal FLCR increased the risk of progression to MM by 3.5 times; RT +/- SE reduced the risk for progression to MM by 75%, confirming that it remains the treatment of choice for SP, whereas ST neither prolonged survival nor reduced the likelihood of SP recurrence or progression to MM.

23. VENETOCLAX FOR PATIENTS WITH RELAPSED/REFRACTORY AL AMYLOIDOSIS

Foteini Theodorakakou[1], Despina Fotiou[1], Vasiliki Spiliopoulou[1], Magdalini Migkou[1], Panagiotis Malandrakis[1], Ioannis Ntanasis-Stathopoulos[1], Maria Roussou[1], Nikolaos Kanellias[1], Evangelos Eleutherakis-Papaiakovou[1], Eirini Solia[1], Asimina Papanikolaou[2], Charikleia Gakiopoulou[3], Maria Gavriatopoulou[1], Evangelos Terpos[1], Meletios-Athanasios Dimopoulos[1], Efstathios Kastritis[1]

[1]Department of Clinical Therapeutics, Alexandra General Hospital, National and Kapodistrian University of Athens, Athens, Greece, [2]Department of Haemopathology, Evangelismos Hospital, Athens, Greece, [3]1st Department of Pathology, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece

OBJECTIVE: The aim of this study is to evaluate the safety and efficacy of venetoclax in relapsed/refractory patients with AL amyloidosis (R/R AL) harboring translocation t(11;14).
METHODS: We analyzed data of 23 consecutive patients with R/R AL, treated in the Department of Clinical Therapeutics, Athens, Greece, who received venetoclax-based therapies.
RESULTS: Among these 23 patients, 21 (91%) were positive for t(11;14). At diagnosis, involvement was: 83% cardiac, 48% renal, 17% liver, 9% nerve and 26% soft-tissue. The Mayo 2004/European stage distribution was 13%/39%/26%/22% for stages 1/2/3A/3B and renal stage distribution was 52%/38%/10% for stages 1/2/3. Median bone marrow infiltration at diagnosis was 20% (range 0-85%), 22% had kappa and 78% lambda LC clones and median baseline dFLC was 346.5 mg/L. At venetoclax initiation, 21 patients (91%) had been exposed to bortezomib and 13 (56.5%) to daratumumab. Median number of prior therapies was 1 (1-3). Six patients (26%) were in hematologic relapse, 13 (56.5%) had inadequate hematologic response and 4 (17%) had persistent organ dysfunction and less than a hemCR. At start of venetoclax, 8 patients (35%) had developed cardiac progression and 12 (52%) renal progression with 3 (13%) on dialysis. Nine (39%) received venetoclax monotherapy, 8 (35%) received venetoclax with low dose dexamethasone and 6 (26%) received venetoclax with daratumumab and dexamethasone. Median time from 1st line to venetoclax was 6.8 months (1.9-109 months); median duration of venetoclax therapy was 5.6 months (0.3-29.5 months) and median dose was 400 mg (200-800 mg). Among evaluable patients (n=17), hematologic response rate was 76%, with hemCR in 7 (41%), hemVGPR in 5 (29%) and PR in 1 (6%); a dFLC<10 mg/L was achieved by 8 (35%). Median time to response was 0.5 months (0.3-6 months). Two patients (9%) had hematologic relapse: 1 during treatment and 1 after discontinuation. Among 13 evaluable patients with cardiac involvement, 3 (23%) achieved a cardiac response and among 7 evaluable patients with renal involvement, 1 (14%) achieved renal response. Regarding adverse events, 9 patients (39%) developed infections (4 Gr 5), 1 (4%) had diarrhea Gr2, 1 (4%) had anemia Gr3 and 2 patients (9%) had thrombocytopenia (Gr2 and Gr4). Dose was reduced in 1 patient (4%) and treatment was discontinued in 4 (17%); reasons for discontinuation were toxicity in 3 patients (13%) and disease progression in 1 (4%). Fourteen patients (61%) are still on therapy. Of the 2 patient that had hematologic progression/relapse, one received further therapy including daratumumab and the other re-started venetoclax. Median follow up of the cohort is 12 months. Eight patients (35%) died, 3 (37.5%) due to AL and 4 (50%) due to infections. Median OS has not been reached; one- and 2-year OS rate was 61%.
CONCLUSION: Treatment with venetoclax induces high rates of complete hematologic response and undetectable MRD in patients with R/R AL. Low rates of organ responses are probably due to short follow-up time and pre-existing advanced organ dysfunction. Despite low risk of cardiac or renal complications, the risk of infections due to immunosuppression should not be underestimated.

24. HYPERFERRITINEMIC SEPSIS IN ADULTS

Sukriye Miray Kilincer Bozgul[1], Devrim Bozkurt[1]

[1]EGE University Faculty of Medicine, Department of Internal Medicine, Division of Intensive Care

OBJECTIVE: There are four uncommon medical conditions characterized by high levels of ferritin, namely the macrophage activation syndrome (MAS), adult onset Still's disease (AOSD), catastrophic antiphospholipid syndrome (cAPS) and septic shock, that share a similar clinical and laboratory features. Hyperferritinemic sepsis (> 500 ng/mL) is associated with increased mortality in single-center studies. In this retospective study, we aimed to evaluate the clinical, demopgraphic features and mortality among hyperferritinaemic and non-hyperferritinaemic sepsis patients.

METHODS: We included patients diagnosed with Sepsis according to the sepsis-3 criteria. The patients complicated with hemophagocytic syndrome, and who have missing data were excluded. Primary end-point was intensive care unit mortality.

RESULTS: Among 225 patients, 153 (68%) patients had serum ferritin leves>500ng/mL. Comorbidities, including history of malignancy was similar among patients who had hyperferritinemia or those has not. Need for vasopressors, SOFA score on sepsis onset, CRP and LDH levels were significantly higher in hyperferritinemic sepsis patients, p=0.001, p=0.001, p=0.002 respectively. Mortality was significantly higher in hyperferritinemic patients, 100(71,4%) vs 40(28,6), p=0.017. Admission ferritin was determined as a predictor of mortality.

CONCLUSION: Hyperferritinemic sepsis is a high-risk hyperinfammatory condition in adult sepsis. Serum ferritin is an easily avaible laboratory marker and early ferritin levels in patients with sepsis are critical in predicting prognosis and planning anti-inflammatory therapies.

POSTER PRESENTATIONS

01. CHRONIC LYMPHOCYTIC LEUKEMIA-ASSOCIATED AUTOIMMUNE HEMOLYTIC ANEMIA: SUCCESSFUL THEAPY WITH OBINUTUZUMAB-VENETOCLAX (OV) COMBINATION

Atakan Turgutkaya[1], İrfan Yavaşoğlu[2], Ali Zahit Bolaman[3]

OBJECTIVE: Due to immune dysfunction and dysregulation, chronic lymphocytic leukemia (CLL) is associated with some autoimmune cytopenias such as immune thrombocytopenia (ITP), autoimmune hemolytic anemia (AIHA) and pure red cell aplasia (PRCA). Patients with CLL who develop these complications are managed similarly with other (non-CLL) patients with these cytopenias. It is suggested to initiate CLL-directed treatment if there is no response. Here, we report a patient diagnosed with CLL with AIHA who remained refractory to conventional treatments and transfusion supports for CLL, but responded to OV therapy.

METHODS: Fifty four-year-old male patient was admitted to the clinic with drenching night sweats. On physical examination, there were cervical and axillary conglomerated lymphadenopathies and massive splenomegaly. Laboratory values were as follows: hemoglobin: 4.2 g/dL, hematocrit: 20.1%, leukocyte: 464,000/mkrL, lymphocyte:419,000/mkrL, and platelet:115,000/mm3, reticulocyte: 0.1016 106/µL (0,026 - 0,095), LDH: 525 U/L (125-243), and direct antiglobulin test(DAT): +4 positive for both ımmunoglobulin (Ig) G and complement(C) 3d. Periperal smear demonstrated an abundance of mature-appearing lymphocytes, basket cells and a few erythrocyte precursor cells. Bone marrow biopsy was also consistent with CLL. He had no deletion 11q or 17p abnormalities assayed by fluorescence in situ hybridization. However, he had deletion 13q mutation. Since there was already an indication for CLL treatment, Rituximab-Fludarabine-Cyclophosphamide (RFC) chemotherapy was administered and he was discharged from hospital thereafter. However, before 2nd cycle of RFC, he was admitted to the emergency room with severe fatigue and cognitive disfunction. Laboratory values were as follows: hemoglobin:2.7 g/dL, hematocrit:9.8%, leukocyte:143,000/mkrL, lymphocyte: 132,000/mkrL, platelet:94,000/mm3, reticulocyte: 0,0762 106/µL, LDH: 835 U/L, and DAT: +4 positive. Since he had life-threatening hemolytic anemia, pulse methylprednisolone (1 gram for three days and 1 mg/kg for following days) was initiated. Despite transfusion support, minimal hemoglobin increase (4 gr/dL) was observed. Meanwhile, his Ig heavy chain mutation status by next-generation squencing was concluded as unmutated (%98.3). Due to this mutation profile and resistant AIHA, his treatment was changed with OV instead of RFC. After the first cycle, his hemoglobin level increased to 10.5 gr/dL, reticulocyte: 0,1457 106/µL, and LDH:274 U/L with DAT negativity. Partial remission of CLL (%50 reduction of spleen size) was achieved two months later.

RESULTS: In the absence of specific guidelines, the therapeutic approach of CLL-associated autoimmune cytopenias is generally experience-based and usually mimics the treatment of primary AIHA. It is suggested that the AIHA generally responds in parallel to CLL therapy. In our case, the possibility of AIHA due to fludarabine cannot be eliminated since there is about 6% incidence of this condition among those receiving fludarabine-based therapy. It has been suggested that targeted agents such as Bruton kinase inhibitors and bcl-2 inhibitors may be beneficial in providing disease control as well as autoimmune complications associated with the same pathophysiological mechanism, although there is limited experience.

CONCLUSION: We presented our case to emphasize the useful effect of OV combination to alleviate hemolysis in parallel to successful control of CLL in this group of patients.

02. CARDIAC TAMPONADE AS THE PRIMARY MANIFESTATION OF HODGKIN LYMPHOMA IN A PREVIOUSLY HEALTHY YOUNG FEMALE

Stavroula Bountola[1], Vasileios Perifanis[1], Michail Makris[1], Triantafyllia Koletsa[2], Charikleia Chatzikosma[1], Erofili Papathanasiou[1], Stylianos Daios[3], Antonios Ziakas[3], Christos Savopoulos[1], Georgia Kaiafa[1]

[1]1st Propedeutic Department of Internal Medicine, Aristotle University of Thessaloniki, School of Medicine, University Hospital AHEPA, Greece, [2]Laboratory of General Pathology and Pathological Anatomy, Aristotle University of Thessaloniki, School of Medicine, Greece, [3]1st Cardiology Department, Aristotle University of Thessaloniki, School of Medicine, University Hospital AHEPA, Greece

OBJECTIVE: Hodgkin Lymphoma (HL) is an uncommon malignancy that is characterized by Hodgkin or Reed-Sternberg cells, constitutional symptoms like weight loss, chills, night sweats, and fever. HL manifests with lymphadenopathy, hepatomegaly, splenomegaly, and pruritus. Cardiac implications of HL remain rarely investigated subjects. There are few case reports in the literature of cardiac tamponade in HL patients. Any pericardial effusion significant for tamponade requires immediate drainage and fluid analysis for thorough investigation. Identification and timely intervention are crucial in addressing these situations.

METHODS: We describe a case of a 21-year-old female patient with cardiac tamponade as an initial HL presentation. The occurrence of cardiac tamponade as the initial presentation of HL is exceptionally rare. All patients described in the literature (Hajra et al 2015, Othman et al 2022 and Azanza JCC et al 2021) were young individuals who presented with symptoms lasting more than a week and cardiac tamponade was the first manifestation of HL.

RESULTS: Case report: A 21-year-old female, without a previous medical history, arrived to the emergency department with chest pain and shortness of breath during the last week. The monitoring showed BP:98/69mmHg, PR:115 beats/min,23 breaths/min and SpO2:97% with a nasal cannula. She demonstrated elevated and distended jugular venous pressure with pulsus paradoxus and muffled heart sounds. Lung auscultation revealed reduced breath sounds at the bilateral lower zones. Electrocardiogram demonstrated sinus tachycardia with low QRS and electric alternans. The transthoracic echocardiography showed a pericardial effusion with right ventricular collapse during diastole and respiratory variation of mitral and tricuspid inflow velocities. The chest X-ray indicated an enlargement of the mediastinum. The patient was admitted to the Coronary Care Unit and emergency pericardiocentesis was performed (600 ml of pericardial fluid were drained). Routine-microscopic findings showed WBC: 56.388K/μL (MONO: 98% and NEU: 2%) without the presence of a microorganism after Gram-stain and acid-fast bacilli stain. Biochemical examination showed total protein: 4.5g/dl (1.5-4.5 g/dl); glucose:61mg/dl (74-100mg/dl) and LDH:411U/L. Blood testing revealed WBC:16000, Hb:9.9g/dL, PLT:411000, normal liver and renal function, LDH:263U/L. Both cytological examination of the pericardial fluid and Histological examination of an excisional biopsy from the pericardium indicated infiltration characterized by lacunar cells (Reed–Sternberg cells), positive immunostaining for CD15 and CD30, confirming the diagnosis of HL. A whole-body CT scan revealed cervical, mediastinal, and paracardiac lymphadenopathy. The patient was classified as stage IV by Ann Arbor and as intermediate-2 (IPS). Combined chemotherapy with standard (ABVD) chemotherapy started and the first cycle was completed. The patient was discharged after 7 days in stable clinical condition. Currently, she has undergone 5 cycles and is being closely monitored for treatment response and potential adverse effects. A PET CT was performed after 5 cycles of chemotherapy and no abnormal findings were observed (complete response).

CONCLUSION: The case gains particular interest due to the initial presentation of cardiac tamponade in a young female patient with an undiagnosed HL. Any pericardial effusion significant for tamponade requires immediate drainage and fluid analysis for thorough investigation. These cases highlight the need for early detection and timely intervention.

03. AI-BASED SURVIVAL PREDICTION IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS

Panagiotis G. Asteris[1], Danial J. Armaghani[2], Amir H. Gandomi[3], Ahmed Salih Mohammed[4], Zoi Bousiou[5], Ioannis Batsis[5], Nikolaos Spyridis[5], Georgios Karavalakis[5], Anna Vardi[5], Evangelia Yannaki[5], Markos Z. Tsoukalas[1], Leonidas Triantafyllidis[1], Gerasimos Konstantakatos[1], Nikos Zygouris[1], Georgios A. Drosopoulos[6], Leonidas Dritsas[1], Nikolaos A. Fountas[1], Nikolaos M. Vaxevanidis[1], Abidhan Bardhan[7], Pijush Samui[7], George D. Hatzigeorgiou[8], Jian Zhou[9], Nikolaos Kotsiou[10], Ioanna Sakellari[5], Eleni Gavriilaki[10]

[1]School of Pedagogical and Technological Education, Athens, Greece, [2]University of Technology Sydney, NSW 2007, Australia, [3]University of Technology Sydney, Sydney, NSW 2007, Australia, [4]American University of Iraq, Sulaimani, Kurdistan-Region, Iraq, [5]G Papanicolaou Hospital, Thessaloniki, Greece, [6]University of Central Lancashire, Preston, UK, [7]National Institute of Technology Patna, Bihar, India, [8]Hellenic Open University, Patras, Greece, [9]Central South University, Changsha, China, [10]Aristotle University of Thessaloniki, Thessaloniki, Greece

OBJECTIVE: The primary objective of this study was to develop a highly accurate predictive model capable of reliably assessing survival outcomes in allogeneic hematopoietic stem cell transplantation (allo-HSCT) recipients. This study sought to address the limitations of current predictive Artificial Intelligence (AI) models by incorporating both pre-transplant and post-transplant parameters, which are often overlooked in existing methodologies. By leveraging Machine Learning (ML) techniques and a comprehensive set of clinical and laboratory variables, we aimed to create a model that not only predicts survival with high accuracy but also identifies the most influential factors affecting patient outcomes. Methods: We compiled a comprehensive database of 564 consecutive patients who underwent allo-HSCT at our JACIE (Joint Accreditation Committee-ISCT & EBMT) accredited unit in George Papanikolaou Hospital between 2015 and 2024. Patient gender, age, disease, disease phase, donor type, Human Leukocyte Antigens (HLA) matching with the donor, graft source, conditioning regimen toxicity, laboratory markers post-HSCT (platelets, lactate dehydrogenase, creatinine at day 2), number of CD34+ cells infused, neutrophil/platelet engraftment, development of acute or chronic Graft-Versus-Host Disease (aGVHD/cGVHD) and secondary malignancy during follow-up and the Disease Risk Index (DRI) were the 18 parameters that were assessed. Additionally, survival status during follow-up was evaluated, thus being the 19th parameter. By utilizing the Data Ensemble Refinement Greedy Algorithm (DERGA), a methodology introduced and successfully applied by our team in the prognosis of COVID-19 severity by utilizing hematological markers and in elucidating the genetic background of COVID-19 patient outcomes, we managed not only to select critical parameters from the database but also evaluate and rank them based on their impact on the outcome of transplanted individuals. For each pattern of input parameters derived from the DERGA algorithm, corresponding predictive models were designed and trained by utilizing a set of classification meta-algorithms accessible within the literature (Extra Trees, Decision Trees, Gradient Boosting, Adaptive Boosting and Cat Boost).
RESULTS: A total of 2,158,875 models were developed and trained, corresponding to 431,775 models for each of the 5 meta-algorithms. The optimal model, utilizing the Extra Trees classification algorithm, achieved an accuracy of 0.9326, based on 7 key parameters: creatinine at day 2, age, aGvHD, disease phase, cGvHD, disease type, and platelet engraftment. The model's accuracy surpassed previously reported models, which achieved lower AUC values (ranging from 0.64 to 0.72) for survival prediction.
CONCLUSION: The DERGA-based model demonstrated high predictive accuracy for survival outcomes in adult allo-HSCT recipients. The model's ability to integrate both pre- and post-transplant variables provides valuable insights for clinical decision-making. This approach outperformed existing models and holds potential for broader applications, including adaptation for pediatric use and prediction of other HSCT-related complications. Future research should focus on multi-center collaborations for external validation and expanding the database to enhance model accuracy.

04. RICHTER'S TRANSFORMATION AT CENTRAL NERVOUS SYSTEM: A RARE PRESENTATION

Ilknur Nizam Ozen[1], Fatma Aykas[1], Firdevs Pelin Eskin[1], Volkan Karakus[1], Erdal Kurtoglu[1]

[1]Antalya Education and Research Hospital

OBJECTIVE: Follicular lymphoma (FL) is an incurable and indolent disease, sensitive to chemotherapeutic agents. FL shows a continuous pattern of relapses with decreasing sensitivity to chemotherapy. There is always a risk for histological transformation to more aggressive malignancies, most commonly diffuse large B cell lymphomas (DLBCL). Here, we present a case with Richter's transformation seen as an involvement of the central nervous system.

METHODS: The patient is a 40-year old woman who had been diagnosed as grade 2 follicular lymphoma 5 years ago. The patient was at stage 4 and had difficulty breathing due to her servical lymph nodes. She was given 6 courses of R-CHOP and 2 years of rituximab maintenance after remission. Four and half years after the diagnosis, she developed signs of recurrence and a re-biopsy was performed from the servical lymph node with a SUV-max of 8.6 as there was a suspicion about Richter's tranformation. The diagnosis was follicular lymphoma and as the disease needed treatment, she was invited for the second line of therapy. She said she had some family issues she has to attend but a few months later, but after a short while she had severe headache and difficulty standing upright. A MRI of the brain revealed 24X40X43 mm mass with a high probability of lymphoma. There was no sign of a cranial mass at CT of the last PET-CT performed 4 months ago. She went under immediate surgery as there was shift to right hemisphere. The pathologic evaluation concluded a Richter's transformation to DLBCL. Marietta protocol was started immediately. She's now receiving her first course of MATRİx protocole.

CONCLUSION: Although very rare, Richter's transformation of follicular lymphoma may appear at central nervous system. At our case, the re-biopsy revealed follicular lymphoma but yet, there was a quick transformation to a high grade lymphoma. Any symptoms regarding the nervous system should be evaluated thoroughly.

05. MAY THE PTPN11 GENE A CANDIDATE GENE IN MYELOPROLIFERATIVE NEOPLASIA?

Burcu Bölük[1], Fatma Keklik Karadağ[2], Sunde Yılmaz Süslüer[1], Cumhur Gündüz[1], Güray Saydam[2], Fahri Şahin[2]

[1]Ege University, Medical Faculty Hospital Department of Medical Biology, [2]Ege University, Medical Faculty Hospital Hematology

OBJECTIVE: BCR-ABL1-negative myeloproliferative neoplasms (MPNs) are a group of clonal myeloid stem cell disorders, which include Polycythemia Vera (PV), Essential Thrombocythemia (ET), and Primary Myelofibrosis (PMF). Genetic markers play a crucial role in diagnosing, monitoring, and treating hematologic malignancies. This study aims to examine gene mutation profiles in cases negative for the JAK2 gene mutation (n=30) among BCR-ABL1-negative MPNs and to identify genetic alterations that contribute to disease progression.

METHODS: DNA samples isolated from peripheral blood of pre-diagnosed MPN cases negative for JAK2 gene mutations were analyzed for variations using the Next-Generation Sequencing (NGS) method. Results: As a result of the study, newly identified variants in all cases were categorized based on their pathogenicity. Next-generation sequencing revealed pathogenic, benign, or likely benign variants located in the exon regions of the SRSF2, U2AF1L5, IKZF1, RUNX3, CDKN2B, TLR4, SMC3, ZRSR2, ASXL1, and INF2 genes. Among the pathogenic or potentially pathogenic variants identified in the newly defined exonic regions, the p.Glu110Val mutation in exon 3 of the PTPN11 gene was found to be common across all cases. Additionally, more than half of the cases exhibited a missense mutation in the GNAS gene, specifically the p.Arg199Pro and p.Asp196Ser changes, both located in exon 8. A novel variant was identified in the CALR gene, which is a known driver mutation for MPN diagnosis, whereas no variants were detected in the MPL gene. Additionally, mutations related to DNA methylation, chromatin modification, and cohesin were observed in the cases. These findings suggest that various mechanisms, including DNA methylation, chromatin modification, and cohesin mutations, contribute to the development of MPNs, highlighting the need for a more comprehensive investigation of the genetic basis of the disease. The growing significance of mutations in MPN treatment necessitates more regular updates to existing diagnostic criteria and prognostic models, as well as a deeper understanding of the mechanisms driving differentiation among MPN subgroups. Conclusion: This study involved mutation profiling of patients who were negative for the JAK2 gene mutation, utilizing a 58-gene sequencing panel. Our investigation revealed a novel and common variation in the PTPN11 gene across all cases studied. Specifically, we identified a missense mutation (p.Glu110Val) in the 3rd exon of PTPN11, which has not been previously documented in any database or literature. While PTPN11 mutations have been reported in pediatric hematologic malignancies and solid tumors, they have not been linked to MPNs until now. Given the consistent presence of this variation in our cases, PTPN11 emerges as a potential candidate gene for targeted treatments in hematologic malignancies. Further studies using next-generation sequencing are recommended to explore the role of PTPN11 in hematologic diseases and enhance our understanding of their underlying mechanisms.

06. BALANCING BLEEDING AND THROMBOSIS IN HEMOPHILIC PATIENTS WITH CORONARY EVENTS

Nikolaos Kotsiou[1], Paschalis Evangelidis[1], Panagiotis Kalmoukos[1], Michail Bolios[1], Zacharo Ntova[1], Sofia Chissan[1], Eleni Gavriilaki[1], Sofia Vakalopoulou[1]

[1]2nd Propedeutic Department of Internal Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece

OBJECTIVE: Hemophilia, an inherited blood clotting disorder, increases the risk of bleeding. While bleeding complications are the primary concern for hemophilic patients, cardiovascular disease can also be a significant comorbidity. Managing coronary events in patients with hemophilia requires a delicate balance between controlling bleeding and preventing thrombotic events. This study aims to analyze the patients with hemophilia who experienced coronary events.

METHODS: A retrospective study was conducted involving 254 patients diagnosed with hemophilia A or B who are registered and monitored in Hemophilia Center of Northern Greece. We further recorded the demographics, bleeding profile, history of cardiovascular disease, treatment during hospitalization and long-term care, and outcome from patients with coronary events.

RESULTS: Out of 254 total hemophilic patients, coronary events have been recorded in 3 individuals. The first patient, a 70-year-old male with mild hemophilia B (factor IX levels 10%), presented with a history of hypertension, chronic obstructive pulmonary disease (COPD) and chronic kidney disease (CKD), but no prior severe bleeding episodes. He was admitted for a non-ST-elevation myocardial infarction (NSTEMI) and received clopidogrel, aspirin (ASA), classical heparin, nitrites, and factor IX (INN-nonacog alfa, 4000 IU per day). He remained hemodynamically stable and asymptomatic throughout his hospitalization, subsequently continuing dual antiplatelet therapy for 6 months, followed by prophylactic factor IX therapy (INN-nonacog alfa, 2000 IU 3 times per week). The second patient, a 61-year-old male with mild hemophilia B (factor IX levels 15%), had a history of nasal bleeding and post-extraction hemorrhage, as well as comorbidities including hyperthyroidism, COPD, dyslipidemia, hypertension, and type II diabetes mellitus. He underwent angioplasty for right coronary artery occlusion and moderate anterior descending stenosis, with factor IX (INN-nonacog alfa) administered pre- and post-operatively. The patient remained stable and asymptomatic, with a recommendation for at least 1 year of dual antiplatelet therapy. At the ages of 67 and 73, he underwent successful open-heart surgery and a subsequent angioplasty, respectively, necessitating the initiation of prophylaxis therapy (2000 IU twice weekly) due to ongoing dual antiplatelet therapy for 1 year. The third patient, a 42-year-old male with severe hemophilia A (factor VIII levels <1%), had a complex medical history including hemarthrosis, septic arthritis, central nervous system (CNS) bleeding, HIV, HCV, and hypertension. He underwent angioplasty with placement of a drug-eluting stent (DES) and received fractionated heparin, tirofiban, and factor VIII. Postoperatively, dual antiplatelet therapy was recommended for 3 months, along with daily factor VIII administration (2000 IU), after which he resumed his prior prophylactic regimen.

CONCLUSION: This study underscores the intricacies involved in managing coronary events in patients with hemophilia, highlighting the necessity of meticulously balancing bleeding risks with thrombotic prevention. Personalized treatment strategies ensured hemodynamic stability and favorable outcomes, illustrating the potential for effective management of coronary complications in this patient population.

07. DETERMINATION OF THE CORRELATION BETWEEN SERUM VCAM-1, ANGPT-1, ANGPT-2, S1P AND OPN LEVELS AND ENGRAFTMENT AFTER AUTOLOGOUS PERIPHERAL STEM CELL TRANSPLANTATION

Ece Yapar Moralı[1], Filiz Vural[2], Mehtap Eğrilmez Yüksel[1], Nur Soyer[2]

[1]Dokuz Eylül University Institute of Health Sciences, Department of Molecular Medicine, [2]Ege University Faculty of Medicine, Department of Internal Medicine, Division of Hematology

OBJECTIVE: We aimed to investigate the changes in serum levels of angiopoietin (ANGPT)-1 and -2, sphingosine-1-phosphate (S1P), osteopontin (OPN) and vascular cellular adhesion molecule (VCAM)-1 during autologous stem cell transplantation (ASCT), their correlation with engraftment and their use as markers for early prediction of engraftment.

METHODS: Fourteen ASCT patients, 5 with lymphoma and 9 with myeloma, were included in the study. Blood samples were collected before the conditioning regimen, on the day of transplantation and 7, 14 and 21 days after transplantation. Cytokine levels were measured by ELISA. $P < 0.05$ was accepted as the statistical significance limit value.

RESULTS: The mean age of the patients was 53.14+12.38 years and 35.7% were female. Total CD34+ cells infused was 6.68±2.33*106/kg, neutrophil and platelet engraftment time was 11.79±2.16 days 16.21±8.76 days, respectively. Compared to baseline, ANGPT-1 levels reached its highest level on day 0, while ANGPT-2 decreased to its lowest level. While OPN increased from day 0, VCAM-1 and S1P reached significantly higher levels from day 14 compared to baseline. We found that the level of ANGPT-2 on day 0 was positively correlated with the day of platelet (PLT) engraftment (r=0.637 and p=0.014). Compared to baseline, ANGPT-1 reached its highest level on day 0, while ANGPT-2 level decreased to its lowest level. OPN was elevated from day 7, while VCAM-1 and S1P reached significantly higher levels from day 14 compared to baseline. We found that the level of ANGPT-2 on day 0 was positively correlated with the day of PLT engraftment (r=0.637 and p=0.014). Day 14 polymorphonuclear leukocyte (PNL) and day 0 ANGPT1/ANGPT2 ratio were strongly positively correlated. Day 14 PLT and day 0 ANGPT2 level were strongly negatively correlated. The area under the curve (AUC) for day 0 ANGPT2 value for predicting a PLT value <20,000/mm3 on day 14 after ASCT was 0.850. The cut-off value was ≥1365 pg/mL (95% CI: 0.000-1.00, p=0.048), with a sensitivity of 75% and specificity of 70%. The AUC for the ANGPT1/ANGPT2 ratio on day 0 for predicting a PNL value >2000/mm3 on day 14 after ASCT was 0.959. The cut-off value was ≥ 3.31 pg/mL (95% CI: 0.000-1.00, p=0.004), with a sensitivity of 83.3% and specificity of 62.5%.

CONCLUSION: Our results support the important role of S1P, OPN and VCAM1, especially ANGPT1 and ANGPT2, in the reconstitution of hematopoiesis after ASCT. We found a strong correlation between PLT engraftment day and day 0 ANGPT2 level and demonstrated that day 0 ANGPT1/ANGPT2 ratio and ANGPT2 level can be used to predict day 14 PNL and PLT level, respectively. Predicting the time to engraftment at day 0 may contribute to treatment development to reduce prolonged hospitalization, infection risk and increased need for blood transfusion due to delayed engraftment. Further studies with more patients are needed to demonstrate the role of cytokine monitoring in predicting delayed engraftment. This research was supported by Health Institutes of Turkey (TUSEB) with the number 2022-ACIL01-31544.

08. EXPERIENCE WITH GEMTUZUMAB OZAGAMYCIN IN RELAPSED AML

Zehra Akşit Bozkina[1], Ajda Güneş[1], Derya Demir[2], Nazan Özsan[2], Mine Hekimgil[2], Emin Karaca[3], Nur Soyer[1], Fahri Şahin[1], Filiz Vural[1], Mahmut Töbü[1], Güray Saydam[1]

[1]Department of Hematology, Faculty of Medicine, Ege University, [2]Department of Pathology, Faculty of Medicine, Ege University, [3]Department of Medical Genetics, Faculty of Medicine, Ege University

OBJECTIVE: Acute myeloid leukemia (AML) consists of disorders representing a genetically diverse heterogeneous group. It is classified on the basis of morphological, cytogenetic, molecular and immunophenotypic characteristics. Although some elderly patients benefit from intensive chemotherapy, being over 75 years of age, renal dysfunction and ECOG score above 2 are factors that increase mortality. Long-term survival in adult patients with AML is only 35%-40% for patients ≤60 years of age, and drops to 5%–15% in patients who are >60 years of age. The majority of patients with AML will have relapsed disease within 3 years. Gemtuzumab ozogamicin (GO) is a humanised anti-CD33 monoclonal antibody linked to calicheamicin, a potent antitumour antibiotic. We are discussing the usability of GO along with three cases of relapsed AML in patients over 65 years old.

METHODS: All our patients are over 65 years old, have experienced septic shock during their hospital stay, received intensive and prolonged infection treatment, are not candidates for allogeneic transplantation, and consist of relapsed/refractory AML cases.ECOG performance scale was 2-3. Unfortunately, two of our cases were lost due to infectious processes. Our other female patient is still alive and is responding to treatment. GO was withdrawn from use in the treatment of AML in 2010 due to its toxic effects and causing premature death. It was put into use again in 2017 with the reorganization of the dosing regimen. GO has been recommended as a first-line treatment for newly diagnosed AML patients. GO alone for newly diagnosed or relapsed/refractory AML GO induces a complete remission (CR) or CR with incomplete platelet recovery (CRp) in up to 25–35% of patients with newly diagnosed or relapsed/refractory AML. Recommendations for the use of GO alone or in combination with doses in newly diagnosed AML cases are available. In patients who undergo intensive chemotherapy, response rates and remission duration are shorter in terms of GO. For patients aged 60 years and older with CD33-positive AML, it has become an alternative treatment when other cytotoxic chemotherapies are not suitable. A study has shown that GO is an effective option for the treatment of relapsed AML with a 31.6% response rate when administered as a single agent. Another study showed that GO had antleukaemic effect in AML patients with NPM1 mutation and significantly reduced the cumulative relapse rate. Although it has been shown to be beneficial in extramedullary involvements according to the literature, unfortunately, myeloid sarcoma developed in one of our cases after GO treatment.

RESULTS: GO is in an important position for the treatment of AML, particularly in patients over 60 years of age who are not amenable to conventional chemotherapy or who have experienced a first relapse. Although initially withdrawn from the market due to observed toxicity, subsequent studies led to its reapproval in 2017 with a revised dosing schedule, aimed at ensuring that the benefits outweigh the risks in a specific population. Although the combinations with cytarabine and daunorubicin recommended in the guidelines could not be applied in the cases we presented, a better response than expected was obtained and experience was obtained without side effects such as HVOD. In relapsed/refractory AML cases, gemtuzumab remains an important agent that may be in a better position.

09. REGRESSION OF SECONDARY ACUTE MEGAKARYOBLASTIC LEUKEMIA (M7) DEVELOPED IN A PATIENT WITH NINE YEAR STANDING MDS; A CASE REPORT

Annita-Ioanna Gkioka[1], Vasiliki Bartzi[1], Alexandros Gkiokas[1], Alexandros Alexandropoulos[1], Aspasia Koudouna[1], Mavra Papadatou-Gigante[1], Marie-Christine Kyrtsonis[1]

[1]Hematology Section, First Department of Propedeutic Internal Medicine, Laikon General Hospital, Athens, Greece

OBJECTIVE: Acute megakaryoblastic leukemia (M7) is an unusual type of acute myeloid leukemia (AML), accounting for approximately 1% of all AML subtypes. Both primary and secondary M7 AML have an extremely poor prognosis. Here, we present the long follow up of an intermediate-risk MDS with fibrosis (MDS-f) that progressed to secondary M7 AML responded to treatment and his disease regressed to MDS –f.

METHODS: Case presentation In 2013, a 74 year old man presented to our department with neutropenia (Neu: 800/μL), macrocytic anemia (Hb: 6,8 g/dl, MCV: 103,6, RTC: 35.000/μL) and thrombocytopenia (PLTs: 59.000/μL). Past medical history included coronary artery disease as well as chronic hepatitis B infection. Bone marrow biopsy revealed trilineage dysplasia with 3% blasts. Karyotype showed the presence of 5q- deletion and the patient was diagnosed with MDS-5q minus, of intermediate risk according to IPSS –R score. The patient initially received lenalidomide with no response and subsequently azacytidine monotherapy. He did not respond for the first 6 months however after the addition of Danatrol he became transfusion-independent after 9 months of treatment. His response was continuous for 8 and a half years. Numerous reevaluations were performed during his follow-up with bone marrow biopsy revealing fibrosis, initially mild (MF-1) that steadily increased and we reclassified the patients as based on WHO 5th edition as MDS-f.

RESULTS: Case description continued In July 2022, the patient presented with anemia (Hgb: 10.1 g/dL), normal platelet count (PLTs: 162 K/μL), normal white count (WBC 9560 K/μL, NEU:5960 K/μL), and increased LDH level (LDH: 1376 U/L). Bone marrow biopsy revealed 70% infiltration of megakaryoblasts (CD61+, CD99+, CD34-, MPO-) along with trileanage dysplasia and grade 3 fibrosis, indicating evolution to megakaryocytic leukemia. Karyotype showed 5q deletion. NGS analysis revealed no pathogenic mutations. After the first cycle of induction treatment with liposomal Daunorubicin/Cytarabine (Vyxeos), the patient achieved complete response with negative MRD (-). However, the patient relapsed after two courses of induction (in December 2022), with 20% megakaryoblasts and 10% myeloblasts in the bone marrow with cells immunophenotype CD34+, CD117+, CD13dim, CD33partial, and HLA-DR+. NGS analysis (15/12/2022) of the clone, indicated the presence of IDH 2 (42% mutation) and SRSF2 (43.5%). He was administrated Gemtuzumab Ozogamicin and achieved complete remission (March 2023) with the bone marrow evaluation revealing the former MDS-f with 5q deletion state. However, as he was still transfusion-dependent he received Danatrol, Lenalidomide, and Peg-Interferon 2alfa and he became almost transfused independent with a stable Hb level of 9 g/dl until today.

CONCLUSION: Our patient with prior MDS-f progressing in secondary AML M7, is still in remission after almost two years. This event free survival is remarkable.

10. COEXISTENCE OF LOW GRADE LYMPHOMA AND POST ESSENTIAL THROMBOCYTEMIA MYELOFIBROSIS, MANAGEMENT OF A CASE REPORT WITH IBRUTINIB

Bahar Sevgili[1], Ajda Güneş[1], Derya Demir[2], Emin Karaca[3], Güray Saydam[1], Nur Soyer[1]

[1]Ege University Hospital, Department of Hematology, [2]Ege University Hospital, Department of Pathology, [3]Ege University Hospital, Department of Genetic

OBJECTIVE: In geriatric population, both myeloprolipherative neoplasms and lymphomas' prevalance increases. In addition, more complex cytogenetic abnormalities are accomplished with different clinical presentations. We aimed to present a case report, with low grade B cell lymphoma (LGBL) infiltration with post essential thrombocytemia myelofibrosis (post-ET MF) in bone marrow and small lymphocytic lymphoma (SLL). He had partial response of lymphoma and was symptomatically stable with ibrutinib

METHODS: A 79 year old man was referred us with constitutional symptoms, loss of appetite. 2 months before administration, he suffered from gastrointestinal (GIS) bleeding. His laboratory findings revealed grade 2 anemia and severely evelated thrombocytes. His GIS endoscopy resulted nonspesific gastritis. On the other hand, his physical examination he had extreme splenomegaly below 10 cm of costal margin. With these findings, he was admitted to our clinic. He also suffered from night sweat and loss of weight. He had no other history of bleeding diathesis, thromboembolic events, fever, cough, dyspnea, constipation, infectious complications. On his physical examination, he had multiple lymphadenopathies in bilateral cervical, axillary, inguinal sides with 40x35 mm maximum diameter. Also he had palpable splenomegaly. His laboratory findings were leucocyte: 19350/µL, neutrophil: 14320 / µL, hemoglobin: 8,6 g/dl and platelets were 876000 / µL, lactate dehydrogenase (LDH): 923 U/L. Other biochemical analysis was unremarkable. His lymph node biopsy was resulted as small lymphocytic lymphoma (SLL) whereas bone marrow biopsy was low grade B cell lymphoma (possibly splenic marginal zone lymphoma) with myelofibrosis. Next generation sequencing analysis was planned.

RESULTS: At the same time, due to his progressive symptoms, he was initially planned for lymphoma treatment with rituximab monotherapy. After 4 courses, his symptoms did not improve, besides his lymph nodes and splenomegaly remained same. We then planned ibrutinib 560 mg/d for lymphoma and unexplained myelofibrosis with thrombocytemia. After 3 months, his platelets were decreased to 500 x103/mm3 as well as his lymph nodes were disappeared and his spleen size was decreased from 220 mm to 150 mm. His NGS analysis resulted with tp53 mutation with variant allele frequency (VAF) of% 15, DIS3 mutation VAF of%20 and KRAS, KMT2D mutations with VAF of%3,5-4. Neither clonal hematopoiesis mutations nor any other well known MPN mutations were detected. His LDH levels regressed to < 1,5x upper limit of normal, and his peripheral blood smear, <%1 blast from the beginning remained. He is still under stable disease with nonpalpable spleen or lymph nodes with good performence status.

CONCLUSION: Within aging, more complex mutations and coexistence of hematological malignancies of different origin occurs more frequently. Our aim for management for these patients is taking under control of disease with least toxicity. Despite his poor genetic alterations, symptomatic management of lymphoma could be handled. It is still unclear whether myelofibrosis management is necessary, on the other hand, he had no sypmtoms or severe cytopenia need for treatment. In conclusion, these patients should be evaluated within symptoms, high risk laboratory findings and finally genetic analysis to choose the most effecive and least toxic management.

11. PROGNOSTIC ACCURACY OF THE DIFFERENT SCORING SYSTEMS FOR ASSESSING MORTALITY IN SEPSIS

Gülçin Çelebi[1], Şükriye Miray Kılınçer Bozgül[2], Ajda Gunes[3], Devrim Bozkurt[2]

[1]Ege University Faculty of Medicine, Department of Internal Medicine, [2]Ege University Faculty of Medicine, Department of Intensive Care, [3]Ege University Faculty of Medicine, Department of Hematology

OBJECTIVE: Disseminated intravascular coagulation (DIC) is a laboratory-based diagnosis due to various critical conditions and sepsis is the most common underlying disease. Recent advances in sepsis-associated DIC management include the development of early diagnostic criteria based on readily available clinical information and the administration of potentially effective anticoagulants. Different scoring systems were used for the diagnosis of DIC and the use of current scoring systems is still controversial. In the present study, we aimed to determined the role of different scoring systems in predicting sepsis mortality.

METHODS: In this single center retrospective study, we included patients > 18 years old who diagnosed with sepsis according to the sepsis-3 criteria between of 2013-2023. We calculated KSTH, ISTH-2001, ISTH-2018, JAAM, JMHW scores for DIC diagnosis and SOFA score for the assessment of organ failure.

RESULTS: Among 131 patients, 62.5% of patient had DIC according to ISTH 2018 criteria, followed by JAAM (63.3%), ISTH 2001 (44.2%), JMHW (48.8%) and lastly KSTH (25.9%). Intensive care unit mortality was 62.5%. Non-survivors had significantly higher DIC scores for all, p<0.005 for each. SOFA scores were also higher in non-survivors, p=0.004. When the scoring results of deceased and surviving patients were evaluated according to the presence of mortality by ROC analysis, cutoff values were as follows: >4 for ISTH 2001; sensitivity 56.10%, specificity 75.51%, AUC:0.666, p<0.001, >4 for ISTH 2008; sensitivity 58.54%, specificity 67.35%, AUC:0. 616, p:0.014, >6 for JAAM; sensitivity 51.22%, specificity 81.63%, AUC:0.660, p:<0.001, >6 for JMHW; sensitivity 63.41%, specificity 75.51%, AUC:0. 709, p:<0.001, >2 for KSTH; sensitivity 36.59%, specificity 91.84%, AUC:0.648, p:<0.001. The cutoff for the SOFA score was >10 with sensitivity 29.7%, spesifity 89.8%, AUC:0.605, p=0.033.

CONCLUSION: Various DIC criteria have demonstrated different performance for the diagnosis and prognosis of sepsis in recent studies. Research with a larger sample size, more comprehensive outcomes, and further confounders is necessary.

KEYWORDS: sepsis, mortality, DIC, prognosis

12. ACQUIRED FACTOR X DEFICIENCY IN LIGHT CHAIN AMYLOIDOSIS (AL): A CASE REPORT OF A PATIENT WITH AL AMYLOIDOSIS AND GASTROINTESTINAL BLEEDING AT DIAGNOSIS FOLLOWED BY AUTOMATIC SPLENIC RUPTURE

Christiana Parisi[1], Kyriaki Kokoviadou[2], Maria Topalidou[2], Vasiliki Kalaitzidou[2], Chrysa Apostolou[2], Athanasios Anastasiadis[2], Anna Xanthopoulou[3], Maria Efstratiadou[2], Anastasia Mpanti[2], Nikolaos Mpalasas[4], Konstantinos Fortounis[5], Sofia Vakalopoulou[6], Efstathios Kastritis[7], Anna Kioumi[8]

[1]PA Haematology Department Pageorgiou Hospital Thessaloniki Greece, [2]Haematology Department Papageorgiou Hospital Thessaloniki Greece, [3]Haematology Department Papageorgiou Hospital Thessaloniki Greece, [4]Surgery Department Papageorgiou Hospital Thessaloniki Greece, [5]Surgery Department Papaeorgiou Hospital Thessaloniki Greece, [6]Haemostasis Department Ippokratio University Hospital Thessaloniki Greece, [7]National & Kappodistrian University Athens, Amyloidosis Center Greece, [8]Hematology Department General Hospital Papageorgiou Thessaloniki Greece

OBJECTIVE: Haemostatic abnormalities are common complications in AL amyloidosis. Bleeding tendency is frequently encountered in AL, while mild subcutaneous hemmorhage is the most common manifestation, life-threatening bleeding has also been reported. Acquired haemostatic abnormalities, including coagulation factor deficiencies, hyperfibrinolysis and platelet dysfunction are the background of bleeding tendency. Acquired deficiency of factor X is the most common coagulation factor deficiency in patients with AL and it is postulated to occur via the absorption of factor X to amyloid fibrils.

METHODS: A 55 year old man presented with fatigue and gastrointestinal bleeding (melena) starting a week before. His laboratory test showed severe anemia, prolonged prothrombin time (PT) and prolonged activated partial thromboplastin time (aPTT). Complete correction on mixing with normal plasma prompted us to proceed with factor assays, which revealed markedly decreased factor X activity at 3%. He had no bleeding history. Immunofixation (serum/urine) showed free λ-light chain. Due to those findings we suspect AL amyloidosis. Bone marrow aspirate and biopsy showed 5% clonal plasma cells and positive cytogenetic abnormality t(11;14). Congo red staining of bone marrow and also of abdominal fat biopsy (two different samples) was negative. He had no hepatosplenomegaly, NT-pro BNP was increased due his history of cardiomyopathy since 25 years. Despite the absence of positive tissue biopsy for amyloid, patient started therapy with bortezomib and dexamethasone and supportive medicine with administration of fresh frozen plasma and human prothrombin complex but without response. Due the present of t(11;14) abnormality we decided as next treatment step to initiate therapy with venetoclax. During the third week of venetoclax administration patient experienced automatic splenic rupture and underwend emergent splenectomy followed by the apropiate vaccination.

RESULTS: Spleen biopsy showed a heavily infiltration of amyloid demonstrated under polarized light. The diagnosis of AL amyloidosis was now established and patient started therapy with daratumumab in combination with venetoclax. Six months after the treatment initiation he improved significantly his clinical and laboratory findings (without hemmorhagic diathesis, improving coagulation tests and decreasing λ -free light chain). It is planned to administrate this combination therapy for two years. Conclusion: Systemic light chain (AL) amyloidosis can lead to an acquired coagulopathy secondary to acquired factor X deficiency. It is no very clear who develops this deficiency in AL amyloidosis and is associated with advanced stage of disease. All patients should be screened for reduced factor X levels. Early recognition and factor replacement is life saving.

13. ADVANCING TRANSLATIONAL RESEARCH: THE BIOBANK OF THE PLASMA CELL DYSCRASIAS UNIT OF THE NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS-UPDATED

Christine Ivy Liacos[1], Nefeli Mavrianou[1], Alexandra Papadimou[1], Konstantina Taouxi[1], Katerina Christostomidou[1], Tina Bagratuni[1], Ioannis Kollias[1], Ioannis Ntanasis-Stathopoulos[1], Panagiotis Malandrakis[1], Vania Spiliopoulou[1], Foteini Theodorakakou[1], Irene Solia[1], Maria Roussou[1], Nikoletta Kokkali[1], Despina Fotiou[1], Evangelos Eleutherakis-Papaiakovou[1], Nikolaos Kanellias[1], Magda Migkou[1], Maria Gavriatopoulou[1], Evangelos Terpos[1], Meletios- Athanasios K. Dimopoulos[1], Efstathios Kastritis[1]

[1]Plasma Cell Dyscrasias Unit, Department of Clinical Therapeutics, National and Kapodistrian University of Athens

OBJECTIVE: The Biobank of the Plasma Cell Dyscrasias Unit started its systematic activity in 2010. Its purpose is the collection of biological samples aimed at translational research, mainly in plasma cell dyscrasias. Our biobank is utilized for genomic, transcriptomic, proteomic, and cellular analysis. Methods: Samples are collected after obtaining written consent and pertain to the framework of routine clinical practice. The samples are mainly from patients with plasma cell dyscrasias, such as multiple myeloma (MM) and monoclonal gammopathy of undetermined significance (MGUS), amyloidosis, and Waldenström's macroglobulinemia. When collecting and processing our samples, we rigorously adhere to Good Clinical Practice (GCP) and Good Laboratory Practice (GLP) in order to avert problems that could jeopardise valuable specimens and compromise years of research. The samples primarily consist of peripheral blood (serum, plasma, and PBMCs), bone marrow (from aspiration, not histological biopsy material), and urine samples (random samples). In relatively few cases, material such as ascites or pleural fluid has been collected. To date, our biobank includes approximately 50,000 samples (not unique, as more than one vial is usually stored from each sampling) from about 2,000 patients who have been assigned a Unique Lab ID. Our biobank samples are also accompanied by the corresponding clinical data (sample annotation), so their utility is maximised within the framework of translational research. The samples are divided and stored according to the following: 1) -20°C: Blood samples for DNA 2) -80°C: Cell pellets, mainly from selected CD138+ and CD19+ cells after bone marrow aspiration, bone marrow plasma (after centrifugation of the aspirate), plasma and serum from peripheral blood, supernatant of ascitic fluid and pleural fluid, fat (sample from aspiration), urine samples. This material is suitable, for RNA and/or DNA extraction. 3) -180°C (liquid nitrogen): Selected CD138+ cells and selected CD19 cells, as well as whole bone marrow mononuclear cells (BMMC's), PBMCs from peripheral blood, cells from pleural or ascitic fluid, stored in DMSO.

RESULTS: Our laboratory collaborates with other laboratories in Greece and abroad. These collaborations include pan-European studies within the framework of the Horizon programs (ELMUMY and Sanguine). Specifically for ELMUMY our BioBank has to date assessed, collected and provided 300 biological samples from individuals with MGUS, sMM, MM which were used for proteomics and transcriptomics. Additional collaborations encompass foreign research centres such as the Dana-Farber Cancer Institute – Harvard Medical School, MD Anderson Cancer Center, Mayo Clinic, University of Turin, University of Navarra, among others. The biobank samples are also used in Greece in collaborations with the Institute of Biomedical Research of the Academy of Athens (IIBEAA), the National Hellenic Research Foundation (EIE), and within the National and Kapodistrian University of Athens (NKUA) such as the Department of Biology, Chemistry, and Pharmacy. Conclusion: The collection of high-quality samples in our BioBank has been proven useful in translational research. These samples are accompanied by detailed clinical data, while consistently respecting our patients. Currently, our laboratory employs 8 scientists who are responsible for managing sample processing, storage and application of translational research.

14. ICANS OR NOT? A CASE REPORT OF BISPECIFIC ANTIBODY USE IN A PATIENT WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM) AND CENTRAL NERVOUS SYSTEM (CNS) DISEASE

Alexandros Alexandropoulos[1], Annita-Ioanna Gkioka[1], Alexandros Gkiokas[1], Mavra Papadatou-Gigante[1], Aspasia Koudouna[1], Vasiliki Bartzi[1], Marie-Christine Kyrtsonis[1]

[1]Hematology Section, First Department of Propedeutic Internal Medicine, Laikon General Hospital, Athens, Greece

OBJECTIVE: Triple- and penta-refractory MM patients carry a dismal prognosis with a median overall survival of <1 year. Novel immunotherapy, in the form of CAR-T cells and bispecific antibodies, has produced impressive responses. Regarding bispecific antibodies, little data has been published on their use in patients with active CNS disease. Here, we present the case of a heavily pretreated MM patient who received talquetamab in our center and who, unbeknownst to us, also had CNS disease. Methods: A 69 year old man with anemia was diagnosed on January 2016 with IgGκ MM, stage ISS 1. The patient received initially lenalidomide/dexamethasone but the treatment was stopped due to ischemic stroke. In October 2017, due to increasing M-protein and new lytic lesions, the patient received 4 cycles of VCd with additional 2 cycles of VRd due to suboptimal response. He then proceeded to autologous-SCT, achieving only a partial response. He received lenalidomide maintenance which was stopped because of IMiD-related rash. He relapsed in 2020 and received DKd, achieving a complete response. In 2023 he relapsed again and Teclistamab was administered, producing CR. However, he relapse under treatment after two months with liver plasmacytoma. He received 2 cycles of DCEP with partial response.

RESULTS: On 04/2024, the patient relapsed again and Talquetamab was administered. Of note, the patient had a negative PET/CT scan 15 days prior to commencing Talquetamab. Less than 24 hours after receiving the first step up dose, the patient had two grand-mal seizures following which he was unresponsive to external stimuli for 48 hours. An MRI scan and lumbar puncture was performed which showed an increased meningeal contrast in the T2 sequence and 500 clonal plasma cells/μl in CSF, respectively. With high methylprednisolone doses, he gradually regained consciousness. Based on ICANS grade system, he would have been assigned stage 4. However, doubt was cast on whether this response was a genuine result of a direct drug action (ICANS) or a tumour lysis response due to the preexisting CNS disease. Talquetamab was abandoned. The patient received 2 cycles of HyperCVAD and intrathecal dexamethazone and Methotrexate achieving CSF response. However, the patient relapsed in June 2024, after almost 4 months with no apparent neurological symptoms. He succumbed to the disease in July 2024.

CONCLUSION: The case illustrates the black box of immunotherapy in patients with unknown CNS relapse. The mainstay imaging method in all stages of MM is the PET/CT scan. However, the default protocol of PET scan covers the area between the base of the skull and the proximal third of the thigh, potentially missing an overt CNS relapse, either in the CSF alone or in combination with plasmacytomas. While the trials testing bispecific antibodies have shown very rare instances of ICANS, there is currently scarce data on CNS penetration as well as the direct effects of the antibody to the brain. As such, more research is needed to elucidate if patients with RRMM slated to start a bispecific antibody should also be checked for CNS disease, irrespective of neurologic symptoms.

15. A CASE OF LIFE-THREATENING ACQUIRED COAGULOPATHY IN CONTRAST TO HYPERVISCOSITY: LYMPHOPLASMACYTIC LYMPHOMA

Neslihan Mandacı Şanlı[1], Mihriban Yıldırım[1], Özge Boyraz1, Ali Ünal[1]

[1]Erciyes University

OBJECTIVE: Waldenstrom's macroglobulinemia (WM), a variant of lymphoplasmacytic lymphoma, is a rare disease characterised by high levels of monoclonal immunoglobulin M (IgM) protein in the blood [1]. Clinical features include anaemia, thrombocytopenia, hepatosplenomegaly, lymphadenopathy and rarely hyperviscosity syndrome [2]. In this report, we aim to contribute to the literature by presenting a case of WM who presented with haemorrhage and prolonged coagulation parameters.

METHODS: A 62-year-old woman, who had been examined at an external centre for abnormal bleeding parameters for about 6 months, presented to the emergency department with the complaint of black defecation. She has had weight loss and abdominal pain for about 4-5 months. White blood cell count was 3.2x10'3/uL (4.8-10.7), haemoglobin 10.3 g/dl (12-16), platelet 198x10'3/ul (130-400), PT (Prothrombin Time) 55.7 s (10-14), INR 5.8 (0.8-1.2), APTT 97.5 s (25-36), Factor V < 5.8%/Factor X < 5.5%/Factor IX 30.6%/Factor 8 < 0.4% (50-150). Coagulation factor inhibitors were positive and no improvement in factor levels in the mixing test. Autoimmune markers were negative and liver and renal function tests were normal. Peripheral blood flow cytometry revealed a B cell group with CD5/CD19-, FMC7+ characterised KAPPA monoclonality in 38% of the lymphoid series. Abdominal ultrasound showed a liver size of approximately 19.5 cm and a spleen size of approximately 20 cm. PET imaging showed uptake in the splenic parenchyma with SUV max: 8.4. The patient had kappa 492 mg/L (6-22), lambda 128 mg/L (8-27), IgM 1318 mg/dL (40-230). The bone marrow aspiration smear showed increased lymphoplasmacytic cells. Immunohistochemistry showed increased polytypic plasma cells with CD38, C138, KAPPA and LAMBDA. We diagnosed LPL in our patient who had high IgM protein, hepatosplenomegaly, anaemia, abnormal coagulation tests and lymphoplasmacytic cell infiltration in the bone marrow. The patient received 3 doses of rituximab 375 mg/m^2 and 1 line of CVP (Vincristine, Cyclophosphamide, Prednisone) chemotherapy. Afterwards, IgM was 35 mg/dL, aPTT was 21.7 s and PT was 14.2 s. Coagulation factor inhibitors were not detected. It was planned to continue treatment with R-CVP.

RESULTS: The LPL is defined as a neoplasm composed of plasmacytoid lymphocytes and plasma cells, usually involving the bone marrow and sometimes the lymph nodes and spleen. It is a very rare disease of unclear etiology [3]. Immunophenotypically, LPL cells usually express CD19, CD20 and kappa light chain. In addition, CD38 and/or CD138 can be used to identify plasma cells. The infiltration of bone marrow and extramedullary sites such as lymph nodes, spleen and liver by malignant B cells and high IgM levels contribute to symptoms associated with pancytopenia, organomegaly and hyperviscosity. Rituximab-based therapy may be the preferred initial treatment for most patients with WM. The use of cyclophosphamide-based therapy may be an appropriate choice when rapid disease control is required.

CONCLUSION: In conclusion, this interesting case with abnormal coagulation tests and factor inhibitor positivity presented with haemorrhage in contrast to other cases of LPL presenting with hyperviscosity syndrome. It should be kept in mind by clinicians that LPL may present with such a clinical pattern.

16. THE FINANCIAL IMPACT OF CLL TREATED WITH BCL-2 INHIBITORS.

Evangelia Kouvata[1], Eleni Tsiara[1], Fotini Karakontaki[2], George Vassilopoulos[1]

[1]Department of Hematology, University Hospital of Larissa, Greece, 2Pharmacy, University Hospital of Larissa, Greece

OBJECTIVE: Chronic lymphocytic leukemia (CLL) is the most common leukemia in the western world. Until recently, therapy was based on a combination of chemo-immunotherapy that almost never resulted in complete remissions (CRs). The introduction of BTKi was a game-changer but these meds also required life-long treatments and never resulted in CRs. The introduction of venetoclax in combination with anti-CD20 antibodies, in the first or subsequent lines, gave us the option of fixed duration treatments with a substantial functional cure rate. Still, fixed duration treatments in the recommended doses, pose a significant financial burden. In this study, we sought to investigate the real-world practices in the treatment of CLL with the novel agents, relative to the cost relief that it confers and the disease outcomes.

METHODS: Overall, we studied 20 pts who fulfilled the criteria for treatment. Eight of these, were 1L patients who received Venetoclax + Obinutuzumab (VenO); for a mean observation period of 23 months, the mean dose was 240 mg QD and all of them were in CR according to iwCLL criteria while 3 of them were also MRD negative. The rest 12 cases were 2L+ and received venetoclax monotherapy for an average of 23 months; in this group, 9 achieved CR, 2 were in partial response and one had disease progression. In this group, the mean dose was 200 mg QD.

RESULTS: When strictly adhering to the protocol, treatment costs are estimated to be in the order 63.000 Euro (E) for patients receiving VenO and 103.000E for those receiving the biannual Ven+Rituximab respectively. However, in the real world setting as presented in this study, the 1L group that received VenO, had a treatment cost per patient in the order of 43.000 representing a 30% reduction from the cost of the approved protocol. In the 2L+ group that received venetoclax monotherapy, the cost per patient was 49.600E representing a nearly 50% reduction in the per-patient cost (estimated at 99.200E).

CONCLUSION: Overall, protocol deviations did not jeopardize the response rates and resulted in a significant cost reduction. It has to be mentioned that dose reductions were mandated by hematological toxicities and not imposed by regulatory agents. Our data indicate that even lower-from-recommended doses of venetoclax can have the desired effect although we cannot argue for the long term efficacy based on our short term observation period.

17. IS OBI-BENDA-LEN A NEW CHANCE TO RELAPSED REFRACTORY B CELL LYMPHOMA PATIENTS?

Denis Bozer[1], Ajda Güneş[1], Derya Demir[2], Nur Akad Soyer[1], Fahri Şahin[1], Filiz Vural[1], Güray Saydam[1]

[1]Ege University Faculty of Medicine, Hematology Department, [2]Ege University Faculty of Medicine, Pathology Department

OBJECTIVE: Treatment of relapsed refractory B-cell lymphomas can be challenging due to previous polychemotherapy and aggressive disease. In this article, we planned to share the results of treatment with Obinituzumab-bendamustine-lenalidomide combination as salvage or bridge therapy in patients with relapsed/refractory B-cell non-hodgkin's lymphoma with aggressive course who received previous treatment. We hypothesized that combining agents that target multiple survival pathways will leverage efficacy
METHODS: Relapsed/refractory (R/R) B-cell NHL patients, with adequate organfunction were eligible. Patients received obinituzumab 1000 mg/day D1, bendamustine 90 mg/m2 D1,2, lenalidomide 20 mg D1-14 every 21 days. PET-CT and CT controls were performed after the 3rd and 6th cycles. Results: Five relapsed/refractory B-cell lymphoma patients who were followed up in our clinic between 2022-2023 were treated with obinituzumab, bendamustin and lenalidomide. Two of these cases were patients with follicular lymphoma refractory to multiple treatments. The other three patients were diagnosed with relapsed refractory diffuse large B-cell lymphoma. The mean age of the cases was 46.4 years (34-72). Two of our patients were female and three were male. Patients had received an average of 2.6 lines of treatment before obi-benda-len treatment (min: 1, max 5 lines treatment). Dose reductions and delays occurredin%10 of cycles, respectively. AEs (% cycles) were the most common and included thrombocytopenia (40%), neutropenia (60%) and anemia (40%). G-CSF was used in all patients and in 90% of cycles, with only 1 case of febrile neutropenia. Two patients had complete response according to Lugano classification after obi-benda-len and two patients had partial response. One patient developed CNS relapse after five cycles of obi-benda-len while all lesions regressed. In one of the patients, obi-benda-len treatment was used as a bridge before allogeneic transplantation and the patient was followed in remission for 1 year after transplantation. Unfortunately, he died due to pneumosepsis. In our 72-year-old patient, although partial response was observed after 3 cycles of obi-benda-len, the protocol could not be continued due to treatment-related severe cytopenias and low ECOG score, and ibrutinib was started as maintenance therapy. The patient died due to sepsis after two cycles of ibrutinib treatment. PFS was observed as 2.5 months on average for 2 patients.
CONCLUSION: Treatment management of relapsed refractory non-hodgkin lymphoma can be quite challenging. Obi -benda-len combination therapy works well in this patient group. The low PFS rates in our patient group are probably due to the fact that we preferred this combination therapy at later stages and acquired mutations due to previous treatments. Choosing it at earlier stages seems to increase the success rate. To accept the validity of this treatment option, studies in more patient groups will be necessary.

18. EVALUATION OF THE SAFETY AND EFFICACY OF DENOSUMAB IN PATIENTS WITH MULTIPLE MYELOMA AND SEVERE RENAL IMPAIRMENT

Evangelos Terpos[1], Ioannis Ntanasis-Stathopoulos[1], Charalampia Kyriakou[2], Carlyn Tan[3], Niels Abildgaard[4], Michel Delforge[5], Dorotea Fantl[6], Cristina João[7], Emilie Carneiro[8], Saad Usmani[3]

[1]Department of Clinical Therapeutics, Alexandra General Hospital, National and Kapodistrian University of Athens, Athens, Greece, [2]Department of Haematology, University College London Hospital, London, UK, [3]Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY, USA., [4]Department of Haematology, Odense University Hospital, Odense, Denmark, [5]Universitaire Ziekenhuizen Leuven, Leuven, Belgium, [6]Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, [7]Department of Hematology, Champalimaud Centre for the Unknown, Lisboa, Portugal Nova Medical School, Universidade Nova de Lisboa, Lisbon, Portugal, [8]Myeloma Lymphoma Research Group-Champalimaud Experimental Clinical Research Programme of Champalimaud Foundation

Objective: Denosumab, a bone-directed agent, has shown non-inferiority to zoledronic acid in the management of multiple myeloma (MM)-related bone disease. As its efficacy and safety in patients with severe RI remains underexplored, this study aims address this gap.

METHODS: The IMWG Bone Subcommittee planned a retrospective study to assess the efficacy and safety of denosumab in MM patients with severe RI, defined as an eGFR based on CKD-EPI of less than 30 ml/min/1.73m^2. A multi-institutional chart review was conducted, analysing data from patients diagnosed with symptomatic MM and RI who were actively receiving treatment and denosumab. Results: Ninety-eight MM patients were included: 51 (52%) newly diagnosed and 47 (48%) relapsed/refractory (RRMM, median of 5 prior treatment lines). The median age was 69 years (IQR 58.0–77.0), and 50 (51.0%) patients were female. All patients had bone disease at baseline and all RRMM patients had previously received zoledronic acid. The median eGFR was 24.0 (16.1-28.0) ml/min/1.73m^2, with 20 patients (20.4%) on dialysis. Renal impairment was due to underlying MM in 72 (73.5%) patients, with concomitant hypercalcemia present in 15 (15.3%) patients. The median follow-up duration was 12.1 (3.3-17.5) months. Eighty-four (85.7%) patients received denosumab at a dose of 120 mg monthly, while 14 (14.3%) received a 60 mg monthly dose. The best responses to MM treatment for the entire cohort were as follows: 8 patients (8.2%) achieved ≥CR, 35 patients (35.7%) vgPR, and 24 patients (24.5%) PR. The median time to best response was 42 days (range 28-90). Regarding renal response, 9 patients (9.2%) achieved CRrenal, 12 patients (12.2%) PRrenal, and 31 patients (31.6%) MRrenal. The median time to renal response was 30 days (range 20-42). As of this report, 44 patients (44.9%) are still undergoing denosumab treatment, while 54 patients (55.1%) have discontinued. The primary reasons for discontinuation were disease progression (58.2%), side effects—primarily hypocalcemia (19.4%), and death. There were 42 recorded deaths (42.9%), with the majority (88.1%) attributed to disease progression. Fifty-one patients (52.0%) experienced hypocalcemia, including 18 cases of grade 1 (35.3%), 13 cases of grade 2 (25.5%), 17 cases of grade 3 (33.3%), and 3 cases of grade 4 (5.9%). This incidence is nearly four times higher than reported for patients with normal renal function or mild to moderate renal impairment. Lower baseline calcium levels (Point-Biserial, β=-0.43, $p<0.001$) and a higher dose of denosumab (120 mg vs. 60 mg; Fisher's p=0.016) were associated with a higher risk of hypocalcemia. Additionally, there were 3 cases (3.1%) of osteonecrosis of the jaw, and no new skeletal-related events (SREs) were reported during the follow-up period.

CONCLUSION: Overall, our findings indicate that denosumab is both effective and safe for MM patients with severe RI, as long as proactive steps are taken to manage hypocalcemia. It is possible that a 60 mg monthly dose may be adequate for preventing both SREs and hypocalcemia in these patients. However, additional prospective research with larger cohorts and extended follow-up is needed to confirm these results and refine treatment guidelines.

19. PROGNOSTIC IMPACT OF T(11;14) IN NEWLY DIAGNOSED PATIENTS WITH MULTIPLE MYELOMA IN THE ERA OF MODERN TREATMENTS

Vasiliki Spiliopoulou[1], Ioannis Ntanasis-Stathopoulos[1], Evangelos Terpos[1], Panagiotis Malandrakis[1], Alexandros Briasoulis[1], Charalampos Filippatos[1], Despina Fotiou[1], Magdalini Migkou[1], Foteini Theodorakakou[1], Nikolaos Kanellias[1], Evangelos Eleutherakis-Papaiakovou[1], Efstathios Kastritis[1], Meletios-Athanasios Dimopoulos[1], Maria Gavriatopoulou[1]

[1]Department of Clinical Therapeutics, Alexandra General Hospital, National and Kapodistrian University of Athens, Athens, Greece

OBJECTIVE: Translocation t(11;14) has been recognized as a significant genetic aberration and is among the most prevalent primary translocations in multiple myeloma (MM). This study aims to evaluate the prognostic significance of t(11;14) in newly diagnosed MM (NDMM) patients, which still remains unclear.

METHODS: Data from 1,007 consecutive patients with newly diagnosed multiple myeloma (NDMM) who were diagnosed and treated in our department between 1997 and 2024, was analyzed. At diagnosis, all patients were tested for t(11;14) using standard fluorescent in-situ hybridization (FISH) in CD138+ selected cells, with positivity defined as at least 20% of clonal cells harboring the translocation. Additionally, the presence of +1q21, t(4;14), t(14;16), del(17p), and del(13q) was also determined by FISH.

RESULTS: At baseline, 70 out of 1,007 patients (6.9%) had the t(11;14) translocation, while 937 patients (93.1%) did not. The median age was 68 years for both groups, with ranges of 32 to 88 years for those with t(11;14) and 33 to 93 years for those without. In terms of gender distribution, 31 patients (44.3%) with t(11;14) and 507 patients (50.3%) without the translocation were male (p=0.15). Overall, there was no statistically significant difference in progression-free survival (PFS) between patients with t(11;14) and those without it [hazard ratio (HR) 1.24, 95% confidence interval (CI): 0.85 – 1.81, p=0.26]. Those with no cytogenetic abnormalities at diagnosis had superior PFS compared to those with t(11;14) (HR 1.52, p=0.04) or any other aberration (HR 1.53, p<0.001). Interestingly, patients with isolated t(11;14) did not show a statistically significant difference in PFS compared to those without any cytogenetic abnormalities [HR 1.16, 95% CI: 0.69–1.93, p=0.58]. However, patients with t(11;14) who also had at least one other cytogenetic abnormality experienced worse PFS [HR 1.95, p=0.02]. Specifically, those with t(11;14) and del(17p) had notably poorer outcomes [HR 3.51, 95% CI: 1.45–8.51, p=0.005], as did those with t(11;14) and del(13q) [HR 4.32, 95% CI: 1.38–13.51, p=0.01]. Overall survival (OS) did not differ between patients with t(11;14) and those without it [HR 1.22, 95% CI: 0.73–2.06, p=0.45]. However, patients with at least one additional cytogenetic abnormality had worse OS [HR 2.57, p=0.005]. On the other hand, patients with t(11;14) did not exhibit inferior OS compared to those without any cytogenetic aberrations [HR 1.62, 95% CI: 0.93–2.81, p=0.09]. Markedly, patients with isolated t(11;14) had similar OS to those without any abnormalities [HR 0.89, 95% CI: 0.39–2.05, p=0.78]. However, the presence of del(13q) [HR 4.20, 95% CI: 1.04–17.01, p=0.04] or del(17p) [HR 4.00, 95% CI: 1.49–10.75, p=0.006] in addition to t(11;14) was associated with significantly worse OS.

CONCLUSION: Isolated t(11;14) in NDMM patients does not appear to be an indicator of poor prognosis with current therapeutic approaches. However, the presence of other high-risk cytogenetic abnormalities is associated with significantly worse outcomes.

20. ISATUXIMAB WITH BORTEZOMIB, CYCLOPHOSPHAMIDE, AND DEXAMETHASONE (ISA-VCD) AS INDUCTION REGIMEN IN NEWLY DIAGNOSED PATIENTS WITH MULTIPLE MYELOMA AND SEVERE RENAL IMPAIRMENT: A PHASE 2 STUDY OF THE GREEK MYELOMA STUDY GROUP

Evangelos Terpos[1], Efstathios Kastritis[1], Sosana Delimpasi[2], Maria Kotsopoulou[3], Konstantina Papathanasiou[4], Vassiliki Labropoulou[5], Eirini Katodritou[6], Ioannis Ntanasis-Stathopoulos[1], Panagiotis Malandrakis[1], Despina Fotiou[1], Magdalini Migkou[1], Foteini Theodorakakou[1], Vasiliki Spiliopoulou[1], Nikolaos Kanellias[1], Evangelos Eleutherakis-Papaiakovou[1], Giorgos Psarros[7], Maria Gavriatopoulou[1], Meletios-Athanasios Dimopoulos[1]

[1]Department of Clinical Therapeutics, Alexandra General Hospital, National and Kapodistrian University of Athens, Athens, Gree, [2]Department of Hematology and Bone Marrow Transplantation Unit, Evangelismos Hospital, Athens, Greece, [3]Department of Hematology, Metaxa Cancer Hospital, Piraeus, Greece, [4]Department of Hematology, Faculty of Medicine, University of Ioannina, Ioannina, Greece, [5]Hematology Division, Department of Internal Medicine, University of Patras, Medical School, Patras, Greece, [6]Department of Hematology, Theagenio Cancer Hospital, Thessaloniki, Greece, [7]Health Data Specialists, Dublin, Ireland

OBJECTIVE: Renal impairment (RI) is a frequent complication of multiple myeloma (MM) associated with poor prognosis. Reversing MM-related RI is crucial for improving survival. Here, we report preliminary results from the EAE116 study, which investigates the effect of Isa-VCd as induction treatment on the renal function of NDMM pts with severe RI and its anti-myeloma effects when followed by maintenance with Isa plus lenalidomide (Len).
METHODS: EAE116 (NCT05147493) is an investigator-initiated, phase 2, prospective, open-label, multicenter study currently underway in Greece, aiming to enroll 51 adult NDMM pts with severe RI, defined as estimated glomerular filtration rate [eGFR] <30 ml/min/1.73m2 or requiring dialysis. The primary endpoint is the renal response rate (RRR) after six months of treatment with Isa-VCd as per the International Myeloma Working Group (IMWG) criteria.
RESULTS: As of 31 May 2024 (data cut-off), 50 pts had received ≥1 dose of Isa-VCd and thus are included in this analysis, of which 37 (74.0%) were still on treatment and 13 (26.0%) had discontinued due to death (7 pts [14.0%]), progressive disease (2 pts [4.0%]), consent withdrawal (2 pts [4.0%]) or physician's decision (2 pts [4.0%]). Median age at baseline was 70.0 years (range 46.0-89.0), with 31 (62.0%) pts being male and 44 (88.0%) having ECOG PS ≤1. Twenty-six (52.0%) pts had stage II and 24 (48.0%) stage III disease as per the revised International Staging System (R-IIS), 7 (14.0%) had high-risk cytogenetics, 14 (28.0%) had lytic bone lesions and 6 (12.0%) had soft-tissue plasmacytomas. Additionally, 11 (22.0%) pts required dialysis. At a median follow-up of 8.5 months (range <0.1-21.2), pts had received a median of 8.0 cycles (range 1.0-23.0). The overall renal response rate (minor response or better) among evaluable pts (44 pts) was 68.2%, with 14 (31.8%) pts achieving PR or better (RRR) and median time to first renal response of 1.2 months (range 0.9-6.1). Among those evaluable for myeloma response (47 pts), the ORR was 83.0% with 57.4% achieving ≥very good partial response (VGPR). The median time to first myeloma response was 1.0 month (range 0.9-11.1). Thirty-seven (74.0%) pts experienced ≥1 treatment-emergent AE (TEAE) and 15 (30.0%) pts ≥1 serious TEAE. Grade ≥3 TEAEs were reported in 18 (36.0%) pts. Most common (≥5%) Gr≥3 TEAEs were pneumonia (8%) and urinary tract infection (6%). Fatal SAEs were observed in 7 pts (14%) and corresponded to respiratory tract infection (2 pts), septic shock (2 pts), pneumonia (1 pt), respiratory failure (1 pt) and aortic aneurysm rupture (1 pt).
CONCLUSION: Induction treatment with Isa-VCd elicits promising myeloma responses in NDMM pts with severe RI. The safety profile is consistent with that of the individual drugs. Infections were the most common Gr≥3 TEAE, which is an expected safety finding in this frail population. We conclude that Isa-VCd may be a new option for NDMM with severe RI.

21. CIRCULATING TUMOR CELLS BY NEXT GENERATION FLOW CYTOMETRY AS A NOVEL PROGNOSTIC BIOMARKER IN PATIENTS WITH MONOCLONAL GAMMOPATHY OF UNDETERMINED SIGNIFICANCE AND SMOLDERING MYELOMA

Panagiotis Malandrakis[1], Ioannis V Kostopoulos[2], Ioannis Ntanasis-Stathopoulos[1], Irene Solia[1], Foteini Theodorakakou[1], Vasiliki Spiliopoulou[1], Despina Fotiou[1], Magdalini Migkou[1], Nikolaos Kanellias[1], Maria Roussou[1], Evangelos Eleutherakis-Papaiakovou[1], Kostantina Taouxi[1], Alexandra Papadimou[1], Christine-Ivy Liacos[1], Maria Gavriatopoulou[1], Meletios-Athanasios Dimopoulos[1], Ourania Tsitsilonis[2], Evangelos Terpos[1], Efstathios Kastritis[1]

[1]Department of Clinical Therapeutics, Alexandra General Hospital, National and Kapodistrian University of Athens, Athens, Greece, [2]Department of Biology, School of Science, National and Kapodistrian University of Athens (NKUA), Athens, Greece

OBJECTIVE: To determine the prognostic significance of circulating tumor cells (CTCs) detected with next-generation flow cytometry (NGF) in patients with Monoclonal gammopathy of undetermined significance (MGUS) and asymptomatic (smoldering) multiple myeloma (sMM).

METHODS: We analyzed the data and outcomes of 254 consecutive patients with MGUS or sMM by IMWG2014 criteria, diagnosed and followed in the Department of Clinical Therapeutics, Athens. Results: The median age of the cohort was 65 years (range 28-87), 60% were females, 118 (46.5%) had non-IgM MGUS and 136 (53.5%) sMM. The isotype was IgG in 83% and 74%, IgA in 16% and 22% and light chain only in 1% and 3% of MGUS and sMM patients, respectively. Among MGUS patients, 46% had abnormal FLC ratio and the median M-spike was 0.59 gr/dl (range: 0-1.87). For sMM patients, 17% had FLC ratio >20, 13% had M-spike >2 gr/dl and 29% had BM plasma cell infiltration >20%. Per IMWGs 20/2/20, 42% were low risk, 32% intermediate and 11% high risk. Cytogenetics were available in 60 patients; 19 MGUS and 41 sMM: t(4;14) was present in 10% of sMM, t(11;14) in 22% of sMM and MGUS, t(14;16) in 8% if sMM, +1q21 in 31% of sMM and 6% of MGUS, del17p in 2% of sMM and 5% of MGUS (one patient each) and del13q in 29% of sMM and 17% of MGUS. CTCs were detectable in 39% patients: 24% of MGUS and 52% of sMM ($p<0.001$). Among those with detectable CTCs, median level was 0.0019% (range 0.0002% to 0.22%) and did not differ among MGUs and sMM patients. The presence of detectable CTCs was associated with higher BM infiltration ($p<0.001$) but did not correlate with sMM risk group: among low-risk patients, 50% had detectable CTCs (median 0.0033%) vs 52% with intermediate (median 0.0031%) and 62% (median 0.0004%) with high ($p=0.864$). The median follow-up was 24 months; 23 patients have progressed and 2-year progression rate was 9% for the whole cohort, 2% for MGUS and 12% for sMM patients. Among sMM patients, 2-year progression rate was 0%, 7% and 15% for low, intermediate and high risk sMM ($p=0.1$). The presence of CTCs was associated with a higher risk of progression to symptomatic MM among all patients in the cohort (HR: 2.99; 95% CI 1.15-7.7, $p=0.024$). Among sMM patients the presence of detectable CTCs was also associated with a higher risk of progression (HR: 2.99; 95% CI 1.02-9.5, $p=0.045$). For MGUS patients the number of events was low to draw statistical conclusions. We also evaluated 0.015% as a CTCs cutoff (identified previously by Termini et al) but did not reach statistical significance.

CONCLUSION: In conclusion, CTCs are detectable in about 39% of patients with asymptomatic monoclonal gammopathies, both in MGUS (24%) and more frequently in sMM (52%). Their presence is associated with increased risk of progression to symptomatic disease, but longer follow up is needed to identify their role in MGUS and the additive information over available risk stratification tools. Longitudinal assessments may provide further prognostic information. CTCs could provide an non-invasive, easy-to-follow biomarker.

22. THE PROGNOSTIC SIGNIFICANCE OF SERUM B2- MICROGLOBULIN LEVELS (SB2M) IN DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL)

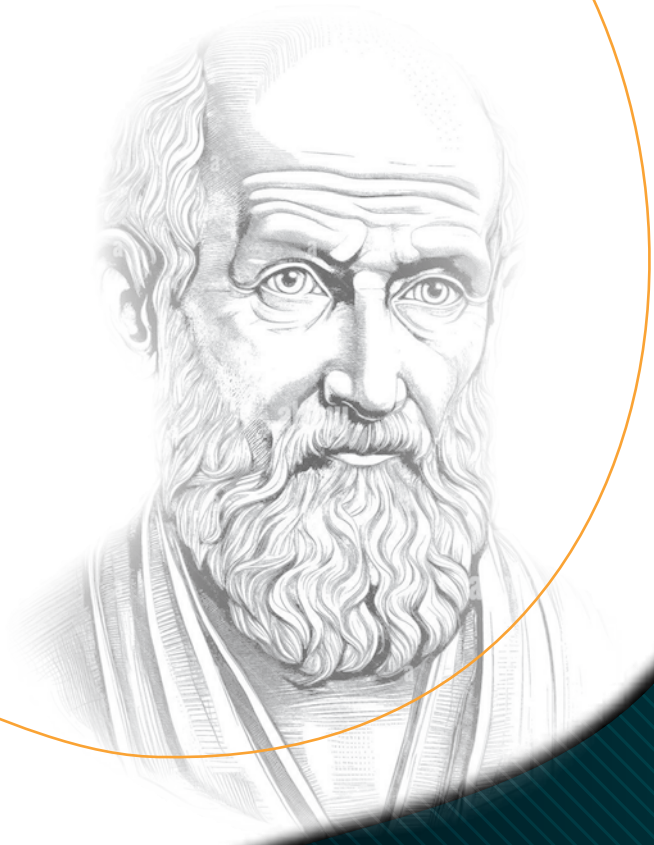
Maria Arapaki[1], Evgenia Verrou[2], Sotirios Papageorgiou[3], Amalia Anastasopoulou[4], Sotirios Sachanas[5], Alexia Piperidou[1], Theodora Triantafyllou[2], Penelope Vryttia[3], Maria Ioakeim[1], Athanasios Liaskas[1], Christina Kalpadakis[6], Marina Siakantaris[1], Maria Dimou[1], Marie-Christine Kyrtsonis[7], Gerassimos Tsourouflis[8], Helen Papadaki6, Kostas Konstantopoulos[1], Vassiliki Pappa[3], Gerassimos Pangalis[5], Panayiotis Panayiotidis[1], Eirini Katodritou[2], Maria Angelopoulou[1], Theodoros Vassilakopoulos[1]

[1]Department of Hematology and Bone Marrow Tranplantation, National and Kapodistrian University of Athens, Laikon General Hospital, Greece, [2]Hematology Department, Theagenio Cancer Hospital, Thessaloniki, Greece, [3]2nd Propaedeutic Department of Internal Medicine, "Attikon" General Hospital, [4]First Department of Internal Medicine, National and Kapodistrian University of Athens, Laikon General Hospital, Athens, Greece, [5]Department of Haematology, Athens Medical Center, Psychikon Branch, Athens, Greece, [6]Department of Haematology, University of Crete, Iraklion, Greece, [7]Second Propaedeutic Department of Internal Medicine, National and Kapodistrian University of Athens, Laikon General Hospital, Athens, Greece, [8]Second Department of Surgery Propedeutic; National and Kapodistrian University of Athens, Laikon General Hospital, Athens, Greece

OBJECTIVE: The International Prognostic Index (IPI) is the standard-but not optimal- tool for prognostication in DLBCL. Sβ2m levels is a well- established prognostic factor for several hematologic malignancies. We aimed to investigate the prognostic significance of sβ2m levels in a large series of homogenously treated DLBCL patients in the rituximab era.

METHODS: We included 1129 patients with DLBCL treated with R-CHOP or similar regimens and selected based on the availability of pretreatment sβ2m levels. Sβ2m levels were analyzed as absolute value measured in mg/L or as the ratio of the observed value to the upper normal limit of the respective laboratory. Sβ2m levels were analyzed as continuous variable in relation to other baseline features. The analysis of the prognostic significance of sβ2mand sβ2m ratio was performed using quartiles (Q1-Q4) or the median value. Freedom From Progression (FFP) was defined as time between treatment initiation and treatment failure (toxic death, primary refractoriness, PR with switch to alternative chemotherapy or relapse); deaths of unrelated causes were censored. Results: The median absolute sβ2m levels were 3.00 mg/L [interquartile range (IQR)2.12-4.53, range 1.05-46.30] and the median sβ2m ratio was 1.33 (IQR 0.95-2.00, range 0.30-20.60). Both sβ2m and sβ2mratio correlated strongly with all baseline features ($p<0.001$). In univariate analysis FFP was significantly worse in patients with high sβ2m (≥median of 3 mg/L) with 2-year FFP of 62.9% vs 84.9% ($p<0.001$). A gradual worsening of FFP was observed from Q1 to Q4 with 2-year FFP rates of 91.9%, 77.7%, 70.0% and 55.6% ($p<0.001$). Similar results of somewhat lower magnitude were observed with sβ2mratio, with 2-year FFP rates of 91.2%, 78.9%, 72.8% and 56.2% for Q1-Q4 respectively ($p<0.001$). The IPI was strongly predictive of FFP, as expected ($p<0.001$). In multivariate analysis, when sβ2m quartiles were analyzed together with IPI (0-1 vs 2 vs 3 vs 4-5), in terms of FFP, both factors had independent prognostic significance ($p<0.001$ for IPI and $p=0.001$ for sβ2m quartiles). Adjusted for IPI, the hazard ratio for Q4, Q3, and Q2 versus Q1 were 2.40, 1.70, and 1.62 (all p-values<0.05). The sβ2mratio was also independent from IPI (hazard ratios for Q4,Q3 and Q2 versus Q1 were 2.88, 2.03 and 2.12).

CONCLUSION: Higher sβ2m Levels was a significant independent predictor of FFP in DLBCL, when adjusted for IPI. A cutoff of 3 mg/L appears reasonable irrespective of the lab reference values, as absolute values were marginally better predictor of FFP compared to values adjusted to the upper normal limit of each lab.



www.ahos2024.com

DROMENA
MEETINGS & EVENTS

LOVI
Tourism & Organization
Working Makes A Difference