Balkan Myeloma Study Group

National and Kapodistrian UNIVERSITY OF ATHENS

EHOD
EGE HEMATOLOJİ ONKOLOJİ DERNEĞİ
AEGEAN HEMATOLOGY ONCOLOGY SOCIETY

EUROPEAN HEMATOLOGY ASSOCIATION

Under the auspices of the EHA SWGMM

10th year ANNIVERSARY

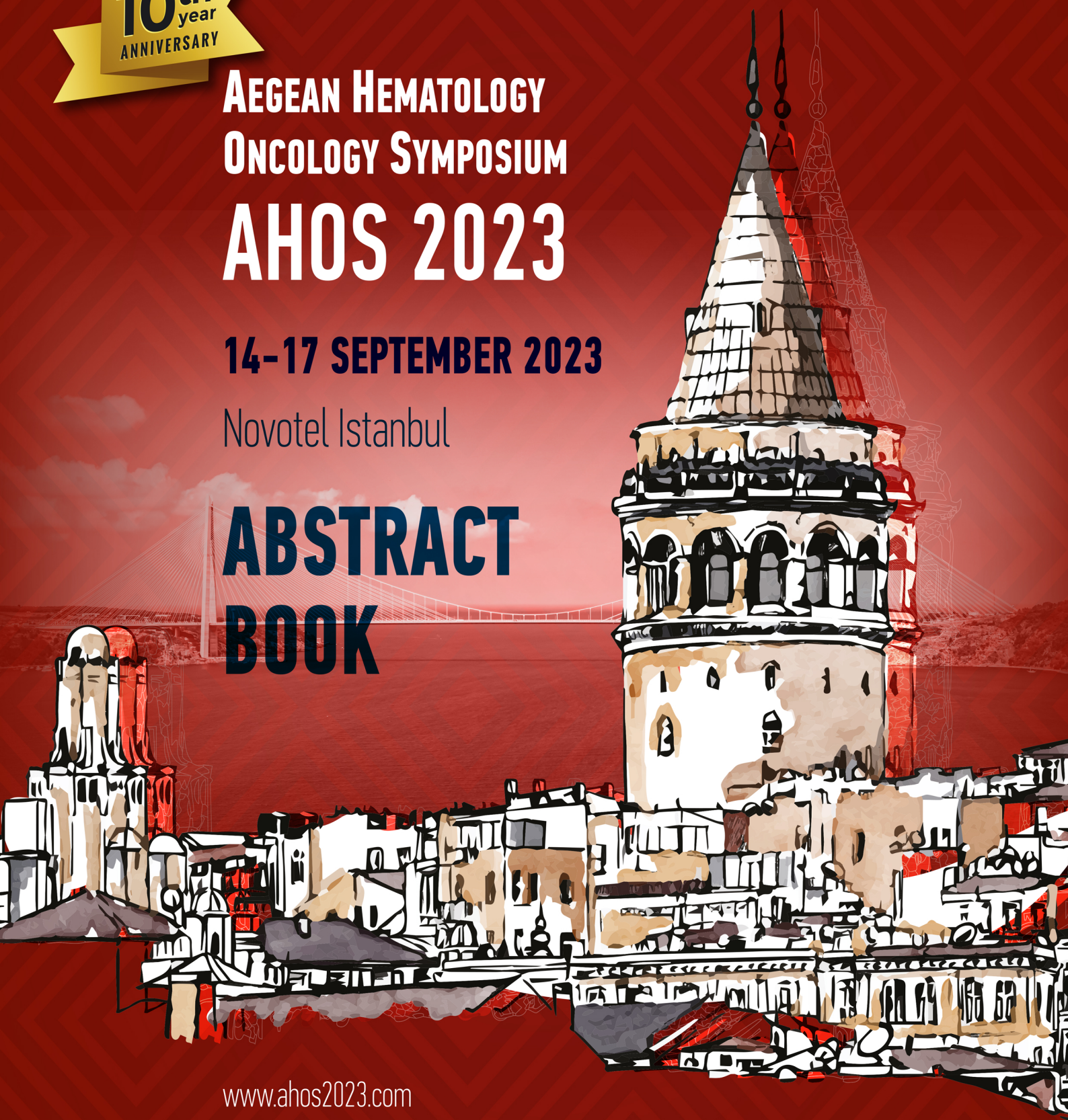
AEGEAN HEMATOLOGY ONCOLOGY SYMPOSIUM

AHOS 2023

14-17 SEPTEMBER 2023

Novotel Istanbul

ABSTRACT BOOK



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10th AEGEAN HEMATOLOGY ONCOLOGY SYMPOSIUM

"AHOS 2023"

14-17 September 2023, ISTANBUL - TURKEY

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EDITORIAL

Dear Colleagues,

*It's a privilege to invite you to the **10th Aegean Hematology Oncology Symposium** which will be held on **14-17 September 2023** in Istanbul, Türkiye. The Symposium is categorized and organized as International Congress under the auspices of the Balkan Myeloma Study Group. It is co-organized by the National and Kapodistrian University of Athens (School of Medicine) in collaboration with the Turkish Medical Association of EHOD (Aegean Hematology Oncology Society). For one more year it is a privilege and a great honor for AHOS to be organized under the auspices of the European Hematology Association, "Scientific Working Group MM".*

This meeting is planned to share country perspectives on Hematology Oncology topics between Greek and Turkish Clinicians, to exchange experiences and to create the basis for multi-center, multi- national studies. During the last years, there was a significant progress in the biology of hematological malignancies that led to the development of several novel drugs in the field. Furthermore, COVID-19 has made several changes in the management of hematology patients, while several complications affecting the blood are developed during COVID-19 or post-COVID-19. The scientific program includes all these data presented by experienced hematologists and it is organized in well-balanced interactive sessions and teaching programs focusing on the needs of Hematology/Oncology Clinicians. This year oral and poster sessions are included again in the program to facilitate the scientific dialogue between Greek and Turkish colleagues and enhance the collaboration between the hematologists of both countries.

We hope that you enjoy the scientific program and we thank you in advance for your contribution in the development of this meeting in order to be even better than the previous AHOS.

On behalf of the Organizing Committee
Evangelos Terpos & Güray Saydam
Co-Chairs

ORAL PRESENTATIONS - AHOS 2023

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A. N. Georgopoulou

06. SOLUBLE CD163 PREDICTIVE OF OVERALL SURVIVAL AND TIME TO TREATMENT IN WM AND LPL.

Alexandros Gkiokas

Second Session

Moderators: *Flora Kontopidou - Mahmut Tobu*

01. IMMUNE THROMBOCYTOPENIC PURPURA AS A HEMATOLOGIC MANIFESTATION OF HIV INFECTION

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Yusuf Ulusoy

03. PERSISTENT BONE MARROW AND IMAGING MRD NEGATIVITY ARE VALUABLE CRITERIA TO STOP LENALIDOMIDE MAINTENANCE FOLLOWING ASCT IN MULTIPLE MYELOMA: RESULTS FROM A PROSPECTIVE COHORT STUDY

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4. PROGNOSTIC SIGNIFICANCE OF CIRCULATING TUMOR CELLS BY NEXT GENERATION FLOW CYTOMETRY IN LIGHT (AL) CHAIN AMYLOIDOSIS

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Maria Gavriatopoulou

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01. IS CONUT SCORE AN INDEPENDENT PROGNOSTİC FACTOR IN PATİENTS WİTH DİFFUSE LARGE B CELL LYMPHOMA?

Denis Çetin

02. HAIRY CELL LEUKEMIA TREATED WITH CLADRIBINE FOLLOWED BY RITUXIMAB: A 3-YEAR SINGLE CENTER EXPERIENCE

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03. METASTATIC MALIGNANT MELANOMA IN BONE MARROW

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01. RETROSPECTIVE ANALYSIS OF CLINICAL FEATURES AND SURVIVAL OUTCOMES IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA

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Ayşe Uysal

ABSTRACTS
ORAL PRESENTATIONS

O1- IMMUNE THROMBOCYTOPENIC PURPURA AS A HEMATOLOGIC MANIFESTATION OF HIV INFECTION

Eren Arslan Davulcu[1]

[1]University of Health Sciences Bakırkoy Dr. Sadi Konuk Training and Research Hospital, Hematology Clinic, Istanbul, Turkey.

Objective : Immune thrombocytopenic purpura (ITP) is an immune-mediated disease, caused by accelerated platelet destruction and inadequate platelet production that results in low platelet counts in the circulating blood. ITP can be a primary condition (primary ITP) or it may be secondary to other conditions (secondary ITP). Human immune deficiency virus (HIV) infection is among the causes of secondary ITP. The study aims to evaluate ITP in patients with HIV infection.

Methods : Patients who were diagnosed with HIV infection while being examined for thrombocytopenia or who were found to have thrombocytopenia during follow-up due to HIV infection were evaluated retrospectively. Patients' age, gender, complete blood count, CD4 count, HIV viral load at diagnosis of ITP, presence of bleeding, treatment for ITP and HIV infections, median time to response for thrombocytopenia, and complications of treatments were recorded. Patients were excluded if they had another cause for thrombocytopenia (medications, another infection, chronic liver disease, etc.,) or pancytopenia. Only those with severe thrombocytopenia (PLT<30× 109/L) evaluated by a hematology specialist were included for further investigation. Complete response (CR) is defined as any platelet count of at least 100 × 109/L, and response (R) is defined as any platelet count between 30 and 100×109/L and at least doubling of the baseline count. No response (NR) is defined as any platelet count lower than 30×109/L or less than doubling the baseline count. The definition of response requires concurrent resolution of bleeding symptoms. Data were reported as frequency (percentage) or median for categorical and continuous variables.

Results : There were 12 HIV-related ITP patients were recruited. Eleven of these patients were male (92%). The median age at ITP diagnosis was 30,5 years (range 22-53). Except for one patient, 11 patients were diagnosed with HIV infection while being examined for thrombocytopenia. This patient, who was diagnosed with ITP after the diagnosis of HIV, was referred for a hematological examination when his thrombocytopenia did not improve despite receiving antiretroviral therapy for 2 months. At the time of diagnosis, 5 patients were asymptomatic for signs of bleeding (42%), 6 patients had petechiae (50%), and 1 patient had hematochezia in addition to mucocutaneous hemorrhages (8%). All patients were started on antiretroviral treatment as recommended by current guidelines, as soon as HIV positivity was detected. Two of the patients were given only antiretroviral therapy without specific therapy for ITP, and the platelet counts were elevated. The remaining 10 patients received ITP-specific therapy in addition to antiretroviral therapy. The median time to the best response was 66 days (range 5-444). The overall response rate in this study was 100%, and there were no relapsed patients. There were no patients who received rituximab or had splenectomy. No significant treatment-related adverse events were reported. Only one patient died and the cause of death is unknown (patient number 2). This patient has never received ITP-specific therapy and is CR for ITP at his last visit.

Conclusion: In this study, it was shown that high remission rates for ITP were achieved with the concomitant administration of treatments for ITP and HIV.

O2- EXPERIENCE OF TOTAL SKIN ELECTRON BEAM RADIOTHERAPY IN PRIMARY CUTANEOUS AGGRESSIVE EPİDERMOTROPIC CYTOTOXIC CD8+ T-CELL LYMPHOMA

Damla Çağla Patır[1],Tayfun Çağrı Hıdımoğlu[2],Ajda Güneş[1],Emine Serra Kamer[2],Yavuz Anacak[2],Özgür Şanlı[3],Mine Hekimgil[4],Nur Soyer[1],Fahri Şahin[1],Güray Saydam[1]

[1]Department of Hematology, Faculty of Medicine, Ege University, [2]Department of Radiation Oncology, Faculty of Medicine, Ege University, [3]Department of Nuclear Medicine, Faculty of Medicine, Ege University, [4]Department of Pathology, Faculty of Medicine, Ege University

Objective : Primary Cutaneous Aggressive Epidermotropic Cytotoxic CD8+ T-Cell Lymphoma (AESTHL) is categorized under the rare subtypes of cutaneous T-cell lymphoma. AESTHL accounts for less than 1% of all CTCL cases. The clinical course of CD8+ AESTHL is aggressive, and the response to chemotherapy is poor. Reported median survival is less than two years.

Methods : Here, we present a rare case of CD8+ AESTHL that achieved improvement in existing lesions after total skin Electron BEAM (TCEB) radiotherapy, following unresponsiveness to combination chemotherapy regimens and autologous stem cell transplantation.

Results : A 44-year-old female patient without a known history of chronic diseases presented to the dermatology department in July 2021 with painful and itchy lesions in the axilla and groin. A skin punch biopsy performed by the dermatology department was evaluated by our university's pathology department, resulting in a diagnosis of cutaneous cytotoxic epidermotropic CD8+ T-cell lymphoma. Considering the localized skin involvement, the patient was started on the CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisolone) chemotherapy protocol. After six cycles, an increase in existing skin lesions and ulceration were observed, and the patient was considered unresponsive to treatment. Allogeneic stem cell transplantation was recommended, but the patient declined. Salvage chemotherapy and followed by autologous stem cell transplantation was planned. After one month, new lesions appeared on the anterior surface of the legs, and a skin biopsy confirmed disease relapse. At this point, the patient was planned to receive ruksolitinib. After the first cycle of ruksolitinib treatment, some improvement was observed in the lesions and reduction in pain; however, afer the second cycle, the lesions and pain recurred. Ruksolitinib treatment was discontinued. TCEB radiotherapy was decided for the patient. The patient received a total of 12 Gray (Gy) / 12 fractions (Fx) radiotherapy, and an additional 1 x 5 Gy radiotherapy was applied to the necrotic lesion on the sole of the foot, which was not included in the total skin area. The patient showed improvement up to 95% in exising lesions after TCEB treatment. However, new lesions reappeared three weeks later. During this period, the existing skin lesions increased again, and respiratory distress developed due to subcutaneous invasion. Palliative radiotherapy with 1 x 5 Gy was applied to the lymphoma infiltration extending into the oral cavity, gingiva, and nasal cavity, resulting in a complete response in the lesion. Following this, a second course of 12 Gy total skin electron therapy was applied, resulting in another complete palliation.

Conclusion: In skin lymphomas, TCEB treatment can serve as a bridge therapy in cases of multi-drug resistance or as a palliative bridge therapy, preventing complications and gaining time for systemic treatment. Treatment can be administered in three phases, with a total of 36 Gy, which further enhances the importance of TCEB as a palliative bridge therapy before transplantation by preventing three cycles of progression. In this case of AESTHL, TCEB treatment intervened when the lesions were progressing rapidly, leading to bleeding, pain, and potential life-threatening complications. The treatment prevented complications, enhanced systemic therapy, and gained time.

O3- PEGYLATED INTERFERON-α IN PATINETS WITH POLYCYTHEMIA VERA AND ESSENTIAL THROMBOCYTHEMIA

Ayşe Uysal[1],**Mustafa Merter**[1]

[1]Fırat University School of Medicine Hematology Department

Objective : In this retrospective study, we aimed to evaluate the efficacy on hematological response, the response generation process and safety of pegylated interferon-α (Peg-IFN) treatment in patients with polycythemia vera (PV) and essential thrombocythemia (ET).

Methods : In this study, 68 patients with diagnosed ET or PV who had received Peg-IFN between May 2016 and May 2022 were enrolled. Reponses rate, adverse effects and response process were evaluated. For the response process, the hematological parameters (the counts of leukocyte, hemoglobin, hematocrit, and thrombocyte) and LDH value at the onset of Peg-IFN were compared with the hematological parameters and LDH value at the 3rd month and 12th month of therapy.

Results : Forty (58,8%) were diagnosed with ET and 28 (41,2%) with PV. Of the all cohorts, 35 (51,5%) of them female and the median age 51,5 (21-81) years at the time of Peg-IFN therapy. The median prior therapy line was 2 (0-3) and the median time from diagnosis to Peg-IFN therapy was 27 (0-226) months. Only 2 patients received Peg-IFN therapy as first-line treatment. In all cohorts, at the median follow-up of 46 (3-79) months, the median duration of Peg-IFN therapy was 21 (1-56) months. The median durations of Peg-IFN therapy in patients with PV and ET were 24 (3-56) months and 20 (1-56) months, respectively. The median duration of Peg-IFN therapy was not statistically different between in patients PV and ET (p=.653). For the response process, concerning leukocyte levels among both ET and PV patients, there was a significant effect of Peg-IFN over time (p=0,026 and p=0.001, respectively). Concerning hemoglobin levels among both ET and PV patients, no significant effect of Peg-IFN over time (p=0,448 and p=0.212, respectively). There was a significant effect of Peg-IFN on thrombocyte levels in patients with ET and PV over time (p=0,0005 and p=0,00005, respectively). Concerning LDH levels among both ET and PV patients, no significant effect of Peg-IFN in time (p=0,097, p=0,949, respectively). In patients with PV, ORR was 53,6%, 85,7%, and 86,6% at the 3, 12, and 24 months. In patients with ET, ORR was 67,6%, 90,9%, and 89,5% at the 3, 12, and 24 months. At 24 months, the CR rate was statistically significantly higher in patients with ET (PV; 33,3%, ET; 79%, p=.016). Currently, 22 patients are receiving Peg-IFN treatment, 15 (22,1%) of them with complete response and 7 (10,3%) with partial response. Treatment was discontinued in 45 (66,2%) patients due to refractory to treatment (33,3%), side effects (42,2%), and inability to obtain medication (22,2%). The most common hematological side effects were neutropenia (16,2%), thrombocytopenia (11,2%), and anemia (11,2%). The most common non-hematological side effects were fatigue (13,2%), fever (11,8%) and headache/dizziness (10,3%). Autoimmune diseases were noted in 3 patients as autoimmune thyroiditis (1 patient), autoimmune thrombocytopenia (1 patient), and autoimmune hemolytic anemia (1 patient).

Conclusion: Peg-IFN is an effective and safe treatment that should be continued for as long as it can be tolerated for the best effect.

O4- IS CONUT SCORE AN INDEPENDENT PROGNOSTIC FACTOR IN PATIENTS WITH DIFFUSE LARGE B CELL LYMPHOMA?

Denis Cetin[1],Fatma Keklik Karadag[2],Nur Akad Soyer[3],Mahmut Tobu[3],Filiz Vural[3],Fahri Sahin[3],Guray Saydam[3]

[1]Ege University Hospital Department of Internal Medicine, [2]Tepecik Training and Research Hospital Department of Hematology, [3]Ege University Hospital Department of Hematology

Objective : The aim of the study was to evaluate the effect of Controlling Nutritional Status (CONUT) score on the prognosis in patients with diffuse large B-cell lymphoma (DLBCL).

Methods : In this study, the data of 209 adult patients who were followed up with the diagnosis of DLBCL at Ege University Hospital Hematology Clinic between 2012 and 2022 were retrospectively analyzed. The CONUT score was calculated based on serum albumin, total cholesterol and lymphocyte levels.

Results : The median age was 60 years. The cut off CONUT was 1. A significant correlation was found between the CONUT score and the presence of stage 1 and 4 disease ($p<0.05$). Bone marrow involvement was present in 4.7% of patients with a CONUT score of ≤1 and in 11.8% of patients with a score of >1 and this relationship was significant ($p<0.05$). A significant correlation was observed between the CONUT score and the prognostic indices ($p<0.05$). There was a significant correlation between CONUT score and overall survival (OS) time ($p<0.05$), but no significant correlation was observed between progression free survival time and CONUT score. Accordingly, while the OS was 55.4±35.7 months in the patient group with a CONUT score of ≤1, it was 45.3±34.5 months in the patient group with a CONUT score of >1. A significant correlation was observed between the 5-year OS and the CONUT score ($p <0.05$). The risk of death was 1.42 (1.02-2.01) times higher in patients with CONUT score >1 than in patients with ≤1 ($p<0.05$).

Conclusion: A high CONUT score is associated with decreased OS, increased bone marrow involvement and extranodal disease.

O5- HAIRY CELL LEUKEMIA TREATED WITH CLADRIBINE FOLLOWED BY RITUXIMAB: A 3-YEAR SINGLE CENTER EXPERIENCE

Fatos Dilan Koseoglu[1],Suayip Korhan[1],Mehmet Can Ugur[1]

[1]Çigli Education and Research Hospital

Objective : Hairy cell leukemia (HCL) is a rare, slow-growing B-cell lymphoproliferative disorder. It is marked by the build-up of B cells with a unique "hairy" appearance in the peripheral blood, bone marrow, and splenic red pulp. Cladribine treatment has been known to lead to complete remission, but relapses are still observed. HCL variant (HCLv), which constitutes about 10% of all HCL cases, does not express CD25 and CD200. Its expression of Annexin1a and CD123 is inconsistent or weak. HCLv shows a poor response to standalone purine analog therapy. However, a combination of cladribine followed by rituximab has shown significant activity and lasting responses, particularly in HCLv patients. This study examines the results of patients with untreated HCL and HCLv who underwent this combination therapy.

Methods : We conducted a retrospective review using patient medical records. Cladribine (5.6 mg/m2) was administered intravenously daily for 5 days, followed about a month later by rituximab (375 mg/m2 IV) weekly for 8 weeks. Response assessments followed standard criteria. Unconfirmed complete remission (CRu) was identified by normalized blood counts and the absence of enlarged organs, without the need for a bone marrow biopsy. Bone marrow evaluations were carried out 12 months post-treatment.

Results : Six patients, with a median age of 49.5 years (ranging from 40.2 to 60 years), achieved an initial CRu. Of these, five were male and one was female. The median follow-up period was 12 months (3-24 months range). One patient was diagnosed with HCLv, showing a lack of CD25, 123, and Annexin1a expressions. All patients tested negative for Hepatitis C, Hepatitis B, and HIV. No patients required hospital stays due to neutropenic fever during treatment. At the time of diagnosis, four patients (or 66.7%) exhibited splenomegaly, and all had some form of cytopenia. Patient baseline characteristics can be found in Table 1. Currently, two patients are still undergoing rituximab treatment, yet they've achieved CRu. Two did not maintain CRu at the 6-month mark. The remaining two are at their 24-month follow-up and have confirmed CR with bone marrow biopsy.

Conclusion: The cladribine-rituximab sequence was safely and effectively administered to all HCL patients at our facility without complications. This approach has shown robust and enduring responses for HCL patients. Those with HCLv, typically less responsive to nucleoside analogs alone, might benefit especially from this strategy. The study's limitations include its retrospective nature, being from a single center, and the limited sample size. Furthermore, detailed mutation analyses of IGHV, BRAF, and MAP2K1—which are crucial for HCLv identification and predicting refractory disease—were not present.

O6- EVALUATION OF SOCIO DEMOGRAPHIC FACTORS AND COMORBIDITIES IN THE PATIENS WITH HEMOPHILIA AT EGE ADULTS HEMOPHILIA AND THROMBOSIS CENTER

Fatma Keklik Karadag[1],Zuhal Demirci[1],Fatoş Dilan Köseoglu[1],Güray Saydam[1],Fahri Şahin[1]

[1]Ege University Department of Hematology and Ege Adult Hemophilia and Thrombosis Center, Izmir, Turkey

Objective : Hemophilia A and B which occur in the deficiency of orderly Factor 8 and 9 are X linked heritable coagulation disorders. The availability of replacement factor products and new treatment strategies over the past seven decades have led to increased life expectancy of the patients with hemophilia. Therefore, the age related morbidities are increased in this population. Both of the comorbities ,that are the reason of hemophilia and age related, affect the quality of life of hemophilia patients. It is known that decreasing the quality of life impress the sociodemografic factors such as education, work and home habitation. Herein, we described the prevelans of comorbidities in patients with hemophilia and seeked the association between socio-demographic factors and hemophilia status.

Methods : 111 Hemophilia A and 24 Hemophilia B patients who were visited Ege adults Hemophlia unit from August 2016 through December 2016, were included in our study. The patients were filled a quastionare form about their socio demographic factors (education, job, inhabitation, marriage, kids and kids' gender, payment, transportation way for the hospital). Retrospectively, we analized the severity of hemophilia according to the factor levels, inhibitör levels, comorbidities, treatment methods, hemophilic arthropathy and viral status.

Results : Mean age was 39,6±1,13 years for 135 hemophilia patients and %60 of all the patients had severe hemophilia disease and patients with severe hemophilia were significantly higher among Hemophilia A (p=0,000). %25 of patients were treated with on-demand therapy and rest of them were treated with prophylaxis therapy. Inhibitor possitivity was found %9,6 among the patients. The patients with hemophilic arthropathy at least one joint were %84,4. Unemployment rate was found %33,3 and %5,6 of patients were student. Nearly half of the patients (%53,3) were living in city center and most of the patiens (%60) were graduated from high school. HCV infection rate was found %9,6 and only one patient with HCV had hepatocellular carcinoma. The prevalence of cardiovascular disease was %6,7; hypertension was %17,8; diabetes mellitus was %13,3. Overweight (Body mass index (BMI) ≥ 25 kg/m2) and obesity (BMI ≥30 kg/m2) patients were %54,1 of all the patients. There is no association between obesity with joint bleeding, annual bleeding rate and hemophilic arthropathy.

Conclusion: Patients with hemophilia usually had some problems in their education and job life because of the bleeding attacks and disability of arthropathy. In our study, the rate of graduation from high school and university is the same as with normal population with the same age. Patients who are working usually do more physical exercise and that is why the bleeding rate is more higher among them. The prevalence of hypertension, cardiovasculary disease and diabetes mellitus in our study patients is similar to normal population of the same age in our country. There is no effect of these comorbidities on bleeding rates, athropathy and severity of hemophilia. It is a challenge for the hematologists to treat older hemophilia patients and manage their developing age related disease because of relatively little experience.

O7- METASTATIC MALIGNANT MELANOMA IN BONE MARROW

Seda Köse[1],Veysel Ürün[2], Demet Kocatepe Çavdar[3], Zehra Narlı Özdemir[4]

İzmir Bozyaka Eğitim Araştırma Hastanesi
İzmir Bozyaka Eğitim ve Araştırma Hastanesi Patoloji Bilim Dalı

Objective : Malignant melanoma is a tumor arising from nevus cells, which is thought to be formed as a result of differentiation of melanocytes. It constitutes 1.2% of all cancer deaths and its frequency is increasing. The organs most frequently metastasized are the central nervous system and the lung. Bone marrow involvement in metastatic malignant melanoma is 20-24%. In this report; we present a 34-year-old patient who was diagnosed with malignant melanoma by bone marrow biopsy while being investigated for lymphoproliferative disease.

Results : A 34-year-old male patient with unremarkable medical history for any chronic condition or medication was admitted with complaints of weakness, weight loss, right cervical swelling and abdominal pain lasting for 1-2 months. The patient, who was referred to us with a preliminary diagnosis of lymphoproliferative disease, was hospitalized in the hematology service for examination purposes. On examination, the patient had a fever and his skin was pale. On palpation, multiple painless, fixed lymph nodes were detected in the anterior cervical and bilateral inguinal regions, the largest of which was 21x12 mm. Abdominal imaging revealed diffuse hypodense lesions in the liver and spleen, diffuse intra-abdominal lymphadenopathy and free fluid. Laboratory findings showed hemoglobin 14.6 gr/dL, white blood cells 9.16 × 109/L, and platelets 238 × 109/L and lactate dehydrogenase 2000 U/L. The blood film was compatible with the blood count without any signs of blastic infiltration. No and fragmentation or hemolysis in erythrocytes. In the differential leukocyte count, neutrophils showed a slight shift to the left - 2% myelocytes, 2% metamyelocytes, 46% polymorphs, 40% lymphocytes, 5% monocytes, and 5% eosinophils. In consultation with interventional radiology, tru-cut biopsy from the mass lesion in the liver segment 6 and 6-7 junction and simultaneously fine needle aspiration biopsy from the cervical lymph node were performed under ultrasound guidance. In the follow-up bone marrow biopsy section performed for diagnostic purposes, cellularity was around 95% and diffuse infiltration consisting of neoplastic cell nests with large, pleomorphic nuclei, prominent eosinophilic nucleoli and occasionally brown pigment containing large eosinophilic cytoplasm suppressing bone marrow cell lines was observed. Immunohistochemical staining features of the infiltrating cells were observed as PanCK (-), CK7 (-), CK20 (-), P16 (-), MelanA (+), S100 (+), HMB45 (+), SOX10 (+). Ki67 was detected 30-35%. Similar findings in the aspiration sample taken from the lymph node. The patient was diagnosed with bone marrow and lymph node metastasis of malignant melanoma. A detailed questioning revealed that a few nevi had beenremoved in the axillary region and on the face a few months ago. There was no exposure to UV light or organic dyes in the past. Finally, the patient was referred to tertiary oncology centerfor the diagnosis of metastatic malignant melanoma and treatment planning.

O8- RETROSPECTIVE ANALYSIS OF CLINICAL FEATURES AND SURVIVAL OUTCOMES IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA

Fatos Dilan Koseoglu[1],Aytur Ayata[1],Mehmet Can Ugur[1]

[1]Bakircay University Cigli Education and Research Hospital

Objective : Chronic Myeloid Leukemia (CML) is a myeloproliferative disorder characterized by the presence of the Philadelphia chromosome, producing the BCR-ABL fusion gene. The BCR-ABL fusion gene leads to abnormal proliferation of myeloid precursor cells and is a hallmark of CML. The majority of patients are diagnosed in the chronic phase. Treatment options for CML have dramatically improved with the introduction of tyrosine kinase inhibitors (TKIs), which have revolutionized the management of CML and significantly improved survival outcomes. However, there is still heterogeneity in treatment responses and long-term outcomes among CML patients. This study aims to retrospectively analyze the clinical characteristics and survival outcomes of CML patients treated at our clinic.

Methods : The medical records of patients diagnosed with CML and treated at Izmir Bakırçay University were retrospectively reviewed. Data on demographics, clinical features, laboratory findings, treatment regimens, and survival outcomes were extracted from the records. Descriptive statistics were used to summarize the clinical characteristics of the study population. Survival outcomes were analyzed using the Kaplan-Meier method. P-values less than 0.05 were considered statistically significant. All statistical analyses were performed using SPSS version 26.0.

Results : Twenty-four patients were involved in the study (Table). The median age of the participants was 57 years, with an interquartile range of 25.2 to 72.7 years. The sample consisted of 14 males and 10 females. A significant portion of the participants had comorbidities: 45.8% had hypertension, 25.0% had diabetes mellitus, and 8.3% had coronary artery disease. At the time of diagnosis, there was a marked neutrophilia. Regarding the blast ratio in bone marrow, 37.5% had a ratio of less than 1%. The reticular fiber ratio showed that 60.9% had a ratio of 1, 34.8% had 2, and 4.2% had 3. For treatment, 91.7% received first-line treatment, and 8.3% received second-line treatment. Among the first-line treatments (n=24), 95.8% received imatinib, and 4.2% received hydroxyurea. In the case of second-line treatments (n=2), 50.0% received dasatinib, and 50.0% received nilotinib. The median duration of follow-up was 21 months (12-63). The response times were consistent across patients, with a median of 30 days for hematologic response, three months for cytogenetic response, and six months for molecular response. Regarding adverse events, 54.2% of participants experienced emesis, 50.0% had edema, 8.3% reported myalgia, 4.2% had diarrhea. On survival analysis, the overall mortality was 8.3%, while there was no disease-related mortality. Median survival time could not be reached (Figure). As deaths were not related to disease itself, any treatment related factor could not be studied.

Conclusion: In conclusion, our retrospective analysis of CML patients treated at our clinic highlights the significance of early diagnosis and the effectiveness of TKI therapy in improving survival outcomes. The data further emphasize the importance of regular monitoring for treatment response and resistance, allowing timely intervention and optimization of treatment strategies.

O9- TP53 GENE MUTATION AND 17P DELETION FREQUENCY IN CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS IN A NEW BASED TERTIARY REFERRAL CENTER

Yusuf Ulusoy[1], Bekir Ayan[2], Öykü Arslan[1], Zeynep Karaali[2], Mesut Ayer[1]

1. Basaksehir Cam and Sakura City Hospital, Hematology Department, Istanbul
2. Basaksehir Cam and Sakura City Hospital, Internal Medicine Department, Istanbul

Aim: We aimed to determine the frequency of TP53 mutation and to examine the relationship between the clinical reflection of TP53 mutation and 17p deletion and two-year survival in newly diagnosed and untreated chronic lymphocytic leukemia (CLL) patients.

Materials and Methods: We retrospectively analyzed newly diagnosed CLL patients referred to Basaksehir Cam and Sakura City Hospital Hematology Department between 2020-2022 years. The demographic characteristics of the patients at the time of diagnosis, laboratory tests, physical examination or imaging records, Rai and Binet stages, TP53 mutation and 17p deletion status, the time they needed the first treatment, the last date of admission to the hospital, and whether they were still alive recorded via the electronic patient registration system.

Results: There were 64 patients in the cohort. In our study, 39 (61%) of 64 patients were. The male/female ratio was calculated as 1.56. The age distribution was between 40 and 81 years and the median age was 63 years. The TP53 mutation, which was examined by the next generation sequencing method, was positive in 5 patients (7.8%). Deletion of 17p, which was examined by fluorescent in-situ hybridization, was positive in 5 patients (7.8%). While 17p deletion was negative in 1 of 5 patients with positive TP53 mutation, 17p deletion was positive in the remaining 4 patients. A statistically significant correlation was found between TP53 mutation and 17p deletion status. There was no statistically significant correlation between TP53 mutation and laboratory findings, lymphocyte doubling time, lymphadenopathy, splenomegaly, hepatomegaly, B symptoms, Rai and Binet staging. While there was a difference in the number of patients received treatment between the TP53 mutation positive group and the TP53 mutation negative group, no statistically significant relationship was found. In addition, although there was a quantitative difference in treatment-free survival (TFS) between the TP53 mutation positive group and the TP53 mutation negative group, no statistically significant relationship was found.

Conclusion: The reason for no significant TFS difference between mutated and non-mutated group was thought to be the number of patients, the small number of samples between the groups and the short follow-up period. In many studies published in the literature, altered TP53 function due to 17p deletion and/or TP53 gene mutation has been associated with poor prognosis and resistance to chemoimmunotherapy in CLL. As a result of our study, TP53 mutation was detected in patients without 17p deletion. In order to better understand the prognostic value of the TP53 mutation, it should be supported by studies with larger number of patients and longer-term clinical follow-up. It is thought that our study will contribute to the literature because it is one of the rare studies in the clinical reflection of TP53 mutation is examined, the incidence of TP53 mutation in newly diagnosed CLL patients in Turkey is determined, and it refers to the relationship between TP53 mutation and 17p deletion.

Key Words: Chronic lymphocytic leukemia, TP53 mutation, 17p deletion

O10- VEXAS SYNDROME : NEW KID IN THE TOWN

Meral Ulukoylu Menguc[1],Tayfur Toptas[1],Asu Fergun Yılmaz[1],Isık Atagunduz[1],Fatma Arıkan[1],Derya Demırtas[1],Ahmet Mert Yanık[1],Ozlem Candan[1],Secil Salım[1]

[1]Marmara University Faculty of Medicine Pendik Training and Research Hospital

Objective : VEXAS syndrome is a novel entity affecting multipl systems which was first described in 2020 in 25 male patients. The clinical picture consists of vacuolinisation in bone marrow progenitors , ubiquitin activating enzyme mutations , X-linked tranmission and autoinflammatory disease . The acronym of the features based the name Vexas syndrome. Herein we present the diagnostic period of a patient with Vexas Syndrome .

Methods : Seventy two years old male patient was referred to hematology with a diagnosis of Sweet Syndrome that was refractory to conventional therapies and macrocytic anemia. Patient suffered joint pain, cutaneous lesions and subfebrile temperature during the past 2 years with an episodic pattern. Joint pain was unresponsive to non-steroidal anti-inflammatory drugs and steroids for the last 2 months. He had biopsy proven Sweet Syndrome exhibiting pale erythematous papulonodular lesions located mainly on extremities .Basal evaluation for malign conditions was normal . After failure of 3 lines of therapy he was followed with prednisolone 5 mg /day and hydroxychlorocine 2x 200mg /day.He had elevated acute phase reactans with normal blood counts initially.During the course he had macrocytic anemia .Peripheral smear showed mild macrocytic anemia. Bone marrow aspiration was normocelluler.Erythroid lineage showed dysplastic features and vacuolinization. Genetics showed lack of myelodysplastic syndrome defining abnormalities. UBA-1 gene exon 3 analysis showed c.121A>C (p.Met41Leu) variant.This somatic variant was considered to be pathogenic in ClinVar and INFEVERS databases for Vexas syndrome. Azacytiditine was commenced and patient is still on therapy with a Hb level of 9,6 g/dl with improved symptoms after 2 courses .

Results : In the first report of Vexas Syndrome 92 % had fever and 88% had skin lesions similar to our case. Each subject received steroids and median 2 lines of synthetic DMARDs before the diagnosis of Vexas Syndrome like our patient received 4 lines of antiinflammatory drugs before the diagnosis. Our patient had a diagnosis of Sweet Syndrome before Vexas diagnosis which was one of the most associated rheumatological condition in the original series. Somatic UBA1 p.Met41Leu variant was the second most common variant which was determined in our case. Bone marrow vaculoinization was limited to erythroid and myeloid progenitors as our case showed vaculoinisation only in erythroid precursors .

Conclusion: Vexas syndrome should be considered in elderly male patients if treatment refractory systemic inflammatory conditions are accompanied by macrocytic anemia.

O11- OPTIMALLY DELIVERED RITUXIMAB DOSE-ADJUSTED EPOCH (R-da-EPOCH) VERSUS RITUXIMAB-CHOP (R-CHOP) IN PRIMARY MEDIASTINAL LARGE B-CELL LYMPHOMA (PMLBCL): A REAL-LIFE COMPARISON WITH CONSECUTIVE HISTORICAL CONTROLS IN A SINGLE CENTER

TP Vassilakopoulos[1],A Piperidou[1],A Liaskas[1],A Kopsaftopoulou[1],ME Lefaki[1],I Vassilopoulos[1],I Drandakis[1],A Georgopoulou[1],K Zerzi[1],A Karapaschalidis[1],A Machairas[1],E Siavou[1],M Belia[1],C Chatzidimitriou[1],E Konstantinou[1],M Arapaki[1],JV Asimakopoulos[1],P Tsaftaridis[1],F Panitsas[1],E Plata[1],M Siakantaris[1],MK Angelopoulou[1],P Panayiotidis[1]

[1]National and Kapodistrian University of Athens, School of Medicine, Laikon General Hospital, Athens, Department of Hematology

Objective : R-CHOP + consolidative radiotherapy (RT) has been historically the usual treatment option for PMLBCL with a cure rate of 75-80%. Current research focuses on increasing efficacy while minimizing RT. The National Cancer Institute introduced the intensified R-da-EPOCH regimen, which produced better outcomes compared to R-CHOP, while minimizing RT. However, there is no direct randomized comparison of R-da-EPOCH vs R-CHOP. A few real-life comparisons demonstrated borderline differences without using optimally selected controls. Such studies are further compromised by the fact that the escalation process is not strictly followed in the real-life and this information is not recorded in detail. The objective of this study was to compare R-da-EPOCH with R-CHOP in patients with PMLBCL of a single, large referral center, where the R-da-EPOCH escalation schedule was strictly followed almost universally.

Methods : We retrospectively analyzed all 35 consecutive patients who received R-da-EPOCH in the Department of Haematology (2017-2022). R-CHOP controls (all R-CHOP-21; R-CHOP-14 not used) were 35 consecutive patients treated at the same Department (or the 1st Department of Internal Medicine prior to May 2008, when the Department of Haematology was founded under the same director), starting from the most recent patient and going backwards (2005-2017). Thus, selection bias was minimized. Consolidative RT was used at the discretion of the treating physician, usually based on PET/CT results, but was systematically avoided after R-da-EPOCH in case of Deauville score 1-4. R-da-EPOCH was given strictly in 33/35 (94%) patients: Two patients reached level 4 and 5 but were not further escalated despite the lack of prohibitive toxicity. Comparably to the original R-da-EPOCH publication 47% received at least level 4, 85% at least level 3 and only 6% just level 1.

Results : Patients' characteristics in the two groups were absolutely comparable except of older age in R-da-EPOCH (median 35 vs 28, p=0.01; ≥38 years 43% vs 9%, p=0.001) and more frequent serous effusions in R-CHOP (37% vs 64%, p=0.03). Relapse/progression was observed in 2 and 11 patients after R-da-EPOCH or R-CHOP, while 2 patients developed therapy-related AML (tAML) after R-da-EPOCH. The 5-year freedom from progression (FFP) was 91% vs 69% (p=0.027). The 5-year event free survival (EFS with tAML counted as events) was 84% vs 69% (p=0.124). The 5-year overall survival (OS) was 97% vs 80% (p=0.063). Among R-CHOP-responders, 20/29 (69%) received RT compared to 2/34 (6%) R-da-EPOCH-responders, both with Deauville score 5. In multivariate analysis -adjusting for age≥38 and serositis or for recently published prognostic models (stage E/IV & LDH≥2x and E/IV & bulky disease)- R-da-EPOCH remained better than R-CHOP regarding FFP [hazard ratios (HR) 0.21-0.26, all p<0.05]. The difference regarding EFS was borderline (HR 0.37-0.45, p~0.10), as well as for OS despite very favourable HRs (HR 0.16-0.18, p=0.09-0.12).

Conclusion: We report for the first time a minimally biased comparison between optimally delivered R-da-EPOCH and R-CHOP-21 with well-matched subgroups of consecutively treated patients. R-da-EPOCH minimized the use of RT in a real-life setting and provided statistically superior disease control than R-CHOP at the expense of 2/35 cases of tAML. EFS and OS benefits were borderline.

O12- PET FOR RESPONSE ASSESSMENT TO R-da-EPOCH IN PRIMARY MEDIASTINAL LARGE B-CELL LYMPHOMA: WHO IS WORTHY TO BE IRRADIATED?

Vassilakopoulos TP[1],Piperidou A[1],Mellios Z[2],Verigou E[3],Katodritou E[4],Kalpadakis C[5],Papageorgiou S[6],Chatzidimitriou C[1],Prassopoulos V[7],Siakantaris M[1],Giatra H[2],Leonidopoulou T[8],Xanthopoulos V[9],Karakatsanis S[10],Hatzimichael E[11],Skoura E[12],Terpos E[13],Pappa V[6],Verrou E[4],Tsirigotis P[6],Symeonidis A[3],Bouzani M[2],Panayiotidis P[1],Angelopoulou M[1],Rontogianni P[14]

[1]National and Kapodistrian University of Athens, School of Medicine, Laikon General Hospital, Athens, Department of Hematology, Athens, Greece, [2]Department of Hematology and Lymphoma, Evangelismos General Hospital, Athens, [3]Hematology Division, Dept of Internal Medicine, University of Patras, Rion, Patras, Greece, [4]Department of Hematology, Theagenion Cancer Hospital, Thessaloniki, Greece, [5]Department of Hematology, University of Crete, Iraklion, Crete, Greece, [6]Second Department of Internal Medicine, Propaedeutic, Hematology Unit, National and Kapodistrian University of Athens, University General Hospital "Attikon", Athens, Greece, [7]Department of Nuclear Medicine, HYGEIA Hospital, Athens, Greece, [8]Department of Hematology, Sismanoglion General Hospital, Athens, Greece, [9]Department of Hematology, HYGEIA Hospital, Athens, Greece, [10]Third Department of Internal Medicine, National and Kapodistrian University of Athens, Sotiria Hospital, Athens, Greece, [11]Department of Hematology, University of Ioannina, Ioannina, Greece, [12]Department of Nuclear Medicine and PET/CT, Vioiatriki, Athens, Greece, [13]Department of Therapeutics, National and Kapodistrian University of Athens, Alexandra Hospital, Athens, Greece, [14]Department of Nuclear Medicine and PET/CT, Evangelismos General Hospital, Athens

Objective : EoT-PET is a valuable tool in the assessment of residual masses in PMLBCL and has been extensively evaluated after R-CHOP or R-MACOP-B. After R-da-EPOCH, the clinical significance of EoT-PET may be different, since most patients with positive scans achieve long-term disease control without radiotherapy (RT). The omission of RT in patients with Deauville 5-point scale score (D5PSS) 4 often causes anxiety to the treating physicians, while handling of patients with D5PSS-5 remains controversial [RT vs high dose chemotherapy/autologous stem cell transplantation (ASCT)].The purpose of the study was to provide an extensive real-world experience on EoT-PET imaging for response evaluation after R-da-EPOCH in PMLBCL, and assess its clinical significance and effect on further treatment guidance.

Methods : Among 145 PMLBCL patients with R-da-EPOCH in 20 Hellenic Centers, 139 were evaluated with EoT-PET and 2 were considered as D5PSS-5 without EoT-PET/CT, since they had progressive disease (PD) at the assumed time of EoT assessment. Cases with D5PSS-4 were retrospectively evaluated by a single nuclear medicine physician and scored visually according to the D5PSS. Freedom from Progression (FFP) was measured from the time of EoT-PET.

Results : Among 141(139+2) EoT-PET evaluable patients, 24 had D5PSS-1(17%), 35 D5PSS-2(25%), 42 D5PSS-3(30%), 22 D5PSS-4(16%) and 17 D5PSS-5(12%) D5PSS-5; including both with frankly PD, who did not undergo EoT-PET. A single patient (0.7%) had D5PSS-X (indeterminate) and was classified as negative. The 5-year FFP for patients with D5PSS-1,2,3,4, and 5 were 95.7%,97.1%,97.5%,86.4% and 29.4%($p<0.001$). D5PSS-1-3:Only 3/102 patients (3%) received RT and only 3/102 relapsed. Two relapses were associated with CNS involvement (unpreventable by mediastinal RT). One patient developed Hodgkin lymphoma and 4 t-AML. D5PSS-4:EoT-PET was available for central review in 20/22 patients. By visual interpretation, 7/20 (35%) were reclassified as D5PSS-3. Only 5/22 received RT and only 3/22 relapsed [5-year FFP 86.4%; 100% versus 82.4% for irradiated versus non-irradiated patients ($p=0.33$)]. Following central review, 2/3 relapses were observed in patients with D5PSS-4,

the third being a patient reclassified as D5PSS-3, who was salvaged with RT and relapsed as Hodgkin lymphoma ~3 years later. FFP rates remained virtually unchanged. Only 3/15 revised D5PSS-4 pts had residual SUVmax>5; 2/3 did not receive RT and both relapsed compared to 0/12 of pts with SUVmax≤5.D5PSS-5: Among 17 patients, 6 had responsive disease by conventional imaging and 11 SD/PD: 5/6 with "responsive D5PSS-5" received RT; all converted to PET-negative and remain in continuous CR (median duration 26 months;range 23-44). All 11 patients with SD/PD ("resistant D5PSS-5") were forwarded to salvage chemotherapy/ASCT. The 5-year OS was 83.3% vs 40.9% for patients with "responsive D5PSS-5" or "resistant D5PSS-5" (p=0.13).

Conclusion: In this large real-life study of R-da-EPOCH in PMLBCL, RT was safely omitted in the vast majority of patients with D5PSS 1-4. The reproducibility of D5PSS-4 was moderate. RT and can be extremely effective when restricted only to the small minority of patients with "responding D5PSS-5"and "high uptake" D5PSS-4 (SUVmax>5), roughly corresponding to just 6% of patients who achieve a conventional response by CTs with R-da-EPOCH.

O13- HOW EARLY PD-1 INHIBITORS CAN INDUCE A COMPLETE METABOLIC RESPONSE IN CHEMOREFRACTORY HODGKIN LYMPHOMA?

A. N. Georgopoulou[1],C. Zerzi[1],V. Samaras[2],Phivi Rondogianni[3],T.P. Vassilakopoulos[1]

[1]Department of Hematology and BMT of the National and Kapodistrian University of Athens, Laikon General Hospital, [2]Department of Radiology, Laikon General Hospital, Athens, Greece, [3]Department of Radiology and Nuclear Medicine, Evangelismos General Hospital, Athens, Greece

Objective : In the KEYNOTE-087 and KEYNOTE-204 trials of pembrolizumab monotherapy in relapsed/refractory classical Hodgkin lymphoma (r/r-cHL) the first formal evaluation for metabolic complete remission (mCR) was performed after the fourth 21-day infusion, specifically after 12 weeks -roughly at 3 months. Thus, we know that the best mCR rate to pembrolizumab monotherapy is ~25-30%, but we do not know how early is that expected to occur.

Methods : To evaluate how early can mCR be achieved through a case report, in which response assessment was incidentally made very early in the course of pembrolizumab monotherapy.

Results : A 24-year-old man with stage IIIB mixed cellularity cHL (MC-cHL) achieved mCR with Deauville 5-point scale score (D5PSS) 1 after ABVDx6. Four years later, he presented with lymphadenopathy and B-symptoms. MC-cHL was reconfirmed. CT-based staging revealed generalized lymphadenopathy and multiple focal spleen lesions. PET/CT revealed extensive, lymphadenopathy (SUVmax=17), multiple left cervical nodes and low uptake in a small right cervical node, multiple bone marrow foci (SUVmax=11), a single liver lesion (SUVmax=5), and splenic lesions (SUVmax=17). Due to drug addiction, the patient was lost to follow-up for 10 months, when he presented in very poor clinical condition with jaundice, B-symptoms, lower limbs' edema and performance status 3. Laboratory testing revealed marked hyperbilirubinemia (direct bilirubin 6.79mg/dL) and elevated liver function tests (LFTs), due to which he received modified salvage therapy with cisplatin and brentuximab vedotin (BV). Hyperbilirubinemia resolved, but, as he felt better, he decided to discontinue treatment. One month later, he presented again with worsening clinical status and received BV-Bendamustine. After two cycles he remained bedridden, with severe hypoalbuminemia, peripheral edema, B-symptoms, and worsening liver dysfunction with serum bilirubin >11 mg/dL. A PET/CT was scheduled prior to pembrolizumab initiation, but his clinical condition rapidly deteriorated. Staging contrast-enhanced CT-scan revealed extensive left supraclavicular and axillary nodes, mediastinal lymphadenopathy, hepatosplenomegaly with multiple subtle hypoattenuating liver and spleen lesions and retroperitoneal lymphadenopathy. Three days after pembrolizumab infusion, the patient experienced a gradual improvement both in clinical condition and LFTs. On day +10 he had a prescheduled appointment for a PET/CT evaluation, which was meant to have been performed prior to pembrolizumab initiation but had been postponed due to the urgent need of treatment. Surprisingly, this very early PET/CT assessment revealed an impressive, nearly mCR with a small residual right cervical lymph node with low-intensity uptake (SUVmax=2.7), still interpreted as D5PSS=4 and raising issues of differential diagnosis between persistent lymphoma versus inflammation. As we were impressed by this unexpected finding of early near-complete resolution of all the hypermetabolic foci, a repeated 18F-FDG-PET/CT was performed on day +21 day from pembrolizumab initiation (prior to cycle 2). At that still very early assessment, a clear mCR was established with D5PSS=1.

Conclusion: The lesson to be learnt from this unique case is that metabolic response to pembrolizumab can be dramatic and clearly evident as early as 10 days after the first infusion and a formal mCR can be demonstrable even just prior to the second infusion, on day +21!

O14- SOLUBLE CD163 PREDICTIVE OF OVERALL SURVIVAL AND TIME TO TREATMENT IN WM AND LPL.

Alexandros Gkiokas[1],Annita Gkioka[1],Mavra Papadatou-Gigante[1],Alexandros Alexandropoulos[1],Vassiliki Bartzi[1],Aspasia Koudouna[1],Thommais Tryfou[1],Nikolitsa Kafasi[1],Marie-Christine Kyrtsonis[1]

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

Objective : As a key component of the bone marrow microenvironment, tumor associated macrophages (TAM) could eventually play a crucial role in the pathogenesis of the hematologic malignancies, such as Waldenstrom's Macroglobulinemia (WM). Hemoglobin scavenger receptor CD163, is a cytokine secreted by TAM, and can be detected in its soluble form (sCD163). Its levels seem to be indicative of TAM's burden and could be used as a potential biomarker for disease progression. In our study, we aimed to investigate whether levels of sCD163 in patients with WM and LPL, correlate with prognosis.

Methods : Out of 194 patients with WM and LPL included in our database, sCD163 was measured in 74 patients, of whom 60 were diagnosed with WM, 8 with IgM-MGUS and 6 with LPL. Clinical and laboratory characteristics were reviewed, after patients' informed consent. Their median age was 64 yrs (range, 33-91), 61% were men and 39% women. Serum sCD163 was tested in frozen sera collected at patients' diagnosis and in 30 healthy individuals (HI) . Measurements were performed by ELISA (Duo-Set R&D Quantiquine) according to the manufacturer's instructions. Median value of variables was used as the cut off point. Median time to treatment (TTT) was 10,5 months (range,1-120) and median overall survival (OS) was 93 months (range, 1-436). Statistical analysis was performed with the SPSS v.26 software.

Results : Median sCD163 was 26826 pg/ml (11831- 97286) in HI, 28163 pg/ml (16696 - 97286) in WM, 26821 (14281-97280) pg/ml in IgM-MGUS, and 27368 (25410-51319) pg/ml in LPL patients. WM and LPL patients with lower levels of sCD163 showed statistically improved 25-years OS (p=0.058) (FIg.1). Additionally, shorter time to treatment was observed in WM patients with sCD163 levels above median (p = 0.05) (Fig.2). A strong correlation was found between sCD163 and other cytokines of the microenvironment of WM; Blys (p=0.0001), sIL6 (p=0.0001), IL10 (p=0.0001), serum syndecan (p=0.0001) (table 1).

Conclusion: Since WM is an indolent yet incurable disease, finding factors that aid physicians predict the prognostication of its course is crucial. Our findings suggest that serum sCD163 levels are able to predict 25-yrs OS and TTT in WM and LPL patients, with higher levels indicating worse prognosis. Elevated sCD163 levels correlate with elevation of other cytokines known to be important for WM pathogenesis (Blys,sIL6 IL10,serum syndecan). sCD163 levels that reflect TAM's burden, could eventually prove to be a significant prognostic marker in WM and LPL.

O15- PERSISTENT BONE MARROW AND IMAGING MRD NEGATIVITY ARE VALUABLE CRITERIA TO STOP LENALIDOMIDE MAINTENANCE FOLLOWING ASCT IN MULTIPLE MYELOMA: RESULTS FROM A PROSPECTIVE COHORT STUDY

Panagiotis Malandrakis[1],Ioannis Ntanasis-Stathopoulos[1],Ioannis V Kostopoulos[2],Maria Gavriatopoulou[1],Foteini Theodorakakou[1],Despina Fotiou[1],Magdalini Migkou[1],Maria Roussou[1],Vassiliki Spiliopoulou[1],Nikoletta-Aikaterini Kokkali[1],Rodanthi-Eleni Syrigou[1],Evangelos Eleutherakis-Papaiakovou[1],Efstathios Kastritis[1],Ourania E Tsitsilonis[2],Meletios A. Dimopoulos[1],Evangelos Terpos[1]

[1]Department of Clinical Therapeutics, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece, [2]Section of Animal and Human Physiology, Department of Biology, School of Sciences, National and Kapodistrian University of Athens, Athens, Greece

Objective : Autologous stem cell transplantation (ASCT) followed by lenalidomide maintenance is the standard of care for eligible patients with newly diagnosed multiple myeloma (MM). Sustained marrow and imaging minimal residual disease (MRD) correlate with prolonged progression-free survival (PFS) and overall survival (OS). It is important to define the optimal duration of maintenance.

Methods : In this prospective study, we included patients with newly diagnosed MM from January 1st, 2016 to December 31st, 2019, who underwent ASCT followed by lenalidomide maintenance. MRD status was assessed in patients who had achieved stringent complete remission (sCR) and then at 6, 12, 24, and 36 months after the initiation of lenalidomide maintenance. MRD samples were evaluated by next generation flow, according to the EuroFlow protocol. Patients, who had at least 3 consecutive MRD negative results and had received at least 36 months of maintenance, underwent a PET/CT scan. If patients had achieved imaging MRD negativity, they discontinued lenalidomide maintenance and MRD was performed every 6 months thereafter. If a patient converted from MRD negative to positive or if the patient relapsed from sCR, lenalidomide maintenance was restarted.

Results : Overall, 151 patients received induction with proteasome inhibitor-based regimens (VCD or VRD) and underwent ASCT. During a median follow-up of 70 months (range 6-84 months) from the time of ASCT, 44 (29.1%) patients had disease progression and 20 (13.2%) patients died. Out of 107 patients who did not progress or die, 42 (39.2%) patients achieved sustained bone marrow MRD negativity and imaging MRD negativity at 3 years after maintenance initiation. Thus, they discontinued lenalidomide maintenance, according to study schedule. Their median age at MM diagnosis was 56 years (range 43-66). Twenty-one (50%) patients were males, whereas 52.4% had IgG, 26.2% had IgA and 21.4% had light chain MM. The patient distribution per ISS was ISS 1 63.4%, ISS 2 19.5% and ISS 3 17.1%, whereas per R-ISS was RISS-1 57.5%, RISS-2 35% and RISS-3 7.5%. The median follow up time from maintenance discontinuation for all patients was 16 months (range 1-31). Six months after discontinuation of lenalidomide maintenance, 39 out of 41 patients were found to be MRD negative. At 12 months post-lenalidomide discontinuation, 36 out of 38 patients continued to be MRD negative. At 18 months, all evaluable patients (n=18) remained MRD negative. At 24 months, 13 out of 14 patients were MRD negative and at 30 months all 4 evaluable patients were MRD negative. Overall, five patients restarted treatment with lenalidomide monotherapy after converting from MRD negative to MRD positive following the initial completion of maintenance, and out of them one patient progressed and received second line of treatment. Only one patient who discontinued maintenance died for reasons not related to multiple myeloma, and with no symptoms of disease progression.

Conclusion: Sustained MRD negativity after ASCT and a completion of 3 years 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.

O16- PROGNOSTIC SIGNIFICANCE OF CIRCULATING TUMOR CELLS BY NEXT GENERATION FLOW CYTOMETRY IN LIGHT (AL) CHAIN AMYLOIDOSIS

Ioannis V. Kostopoulos[1],Despina Fotiou[1],Foteini Theodorakakou[1],Eirini Solia[1],Pantelis Rousakis[1],Chrysanthi Panteli[1],Vassiliki Spiliopoulou[1],Magdalini Migkou[1],Asimina Papanikolaou[1],Harikleia Gakiopoulou[1],Evangelos Terpos[1],Ourania Tsitsilonis[1],Meletios A. Dimopoulos[1],Efstathios Kastritis[1]

[1]Department of Clinical Therapeutics, Plasma Cell Dyscrasia Unit, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece

Objective : In light chain (AL) amyloidosis a plasma cell clone produces monoclonal light chains that form amyloid fibrils deposited in organs and causing tissue toxicity. Circulating tumor cells (CTCs) detected by next generation flow cytometry (NGF) in monoclonal gammopathy of undetermined significance (MGUS) or asymptomatic multiple myeloma (MM) are associated with high probability of becoming symptomatic, while in symptomatic MM patients, CTCs is a negative, independent, prognostic factor. We aimed to evaluate the prognostic and biological impact of CTCs in treatment-native patients with AL amyloidosis using the highly sensitive NGF.

Methods : The analysis included 158 consecutive patients with AL amyloidosis evaluated for the presence of CTCs in peripheral blood (PB) according to EuroFlow guidelines. Two independent 8-color panels were used, both of which containing CD19-PC7, CD27-BV510, CD38-FITC, CD45-PerCPCy5.5, CD56-PE, CD138-BV421; in addition, CD117-APC and CD81-APCC750 were used only in the surface tube or CyIgκ-APC and CyIgλ-APCC750 only in the intracytoplasmic tube. A median number of 5 million events (range 3.9x106-6.1x106) were acquired for each tube with median limit of detection (LOD) 2.3x10-6 (range 2x10-6-3.1x10-6).

Results : The median age of the patients was 67 years (38-87), 57% were males; 86% had cardiac and 56% renal involvement. According to Mayo staging, 13%, 33% and 54% of patients were classified as stage 1, 2 and 3, respectively, while 20%, 57% and 23% were rated as renal stage 1, 2 and 3. Median iFLC and dFLC levels were 299.3 mg/dL and 288.5 mg/dL. Bone marrow (BM) infiltration was 10% (range 0-60%) and the most common cytogenetic finding by FISH was t(11;14) in 46% of the patients. 96% of the cohort received bortezomib-based treatment while 34% of patients were treated with daratumumab. CTCs were detectable in 57% of patients and the median level of CTCs (detectable) was 0.0024% (range 0.0002%-11.4%); only 15 (9.5%) patients had CTCs > 0.02% (which has prognostic significance in MM). Patients with detectable CTCs had higher levels of LDH, iFLCs, BM infiltration and NTproBNP and there was a correlation among the levels of detectable CTCs with iFLCs ($p<0.001$) and BM infiltration ($p<0.001$). CTCs were present more often in patients with +1q21 ($p=0.022$); interestingly, their levels patients were higher compared with patients with CTCs but without +1q21 ($p=0.014$). 59 patients (37%) were evaluated for MRD in the BM by NGF; among MRDneg patients, 80% had no detectable CTCs at diagnosis; no patient with CTCs at diagnosis ≥10-4 achieved MRD negativity. Presence of CTCs did not affect overall survival (OS). Different cutoffs of CTCs had no statistically significant prognostic impact, even after adjustment for Mayo stage, nevertheless, patients with detectable CTCs had lower probability of CR/VGPR at 3 months (57% vs 75%, $p=0.049$).

Conclusion: NGF is a highly sensitive method that can detect CTCs in 57% of patients with AL amyloidosis. Even though the presence of CTCs is associated with adverse prognostic parameters, by themselves CTCs did not affect the prognosis of AL amyloidosis, as the extent of the cardiac impairment has the leading role in prognosis.

O17- EVALUATION OF EARLY PROGRESSIVE DISEASE (EPD) IN NEWLY DIAGNOSED MYELOMA PATIENTS AND IDENTIFICATION OF PROGNOSTIC FACTORS IN THE ERA OF MODERN THERAPIES. THE GREEK MYELOMA STUDY GROUP EXPERIENCE.

Eirini Katodritou[1],Dimitra Dalampira[1],Efstathios Kastritis[2],Fotini Theodorakakou[2],Despina Fotiou[2],Sosana Delimpasi[3],Emmanouil Spanoudakis[4],Ioannis Ntanasis-Stathopoulos[2],Theodosia Papadopoulou[1],Aggeliki Sevastoudi[1],Theodora Triantafyllou[1],Aikaterini Daiou[1],Vasiliki Palaska[1],Kyriaki Tsirou[1],Nikolaos Karampatzakis[1],Anastasia Pouli[5],Magda Migkou[2],Maria Gavriatopoulou[2],Evgenia Verrou[1],Marie Christine Kyrtsonis[6],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 and Bone Marrow Transplantation Unit, Evangelismos Hospital, Athens, Greece, [4]Department of Hematology, University Hospital of Alexandroupolis, Alexandroupolis, Greece, [5]Department of Hematology, Agios Savvas Cancer Hospital, Athens, [6]First Department of Propaedeutic Internal Medicine, Laikon General Hospital, National and Kapodistrian University of Athens, Athens, Greece

Objective : Despite treatment improvements there is still a respectable proportion of newly diagnosed multiple myeloma (MM) patients that experience early progressive disease (EPD) defined as relapse or progression <18 months from start of therapy. Herein we describe the clinical characteristics and outcomes of patients with EPD and examine the prognostic ability of staging systems, molecular cytogenetics, and type of upfront treatments, in the current therapeutic landscape.

Methods : We evaluated 1436 newly diagnosed MM (M/F: 700/736; median age: 67, range 29-90) with complete data for international staging system (ISS) and R-ISS. All patients had achieved at least MR to primary therapy and had complete data regarding 1st line treatment and outcomes. Comparisons of patients' characteristics was performed with Mann-Whitney-U test, One-Way-ANOVA and X2. A binary logistic regression analysis was performed to determine significant prognostic factors for EPD; $p<0.05$ was considered as statistically significant.

Results : Early progressive disease was observed in 335/1436 (23.3%). Patients with EPD had higher median age, β2-microglobulin, LDH and bone marrow infiltration and lower hemoglobin and eGFR, compared to non-EPD ($p<0.05$); ISS-3 and RISS3 were more frequent in patients with EPD (34% vs. 26%; $p<0.001$ and 19% vs. 10%; $p<0.001$, respectively). Data for second revision of ISS (R2-ISS) was available in 73% of patients: R2-ISS III and IV were more frequent in patients with EPD (63% vs. 42%; $p<0.001$). Presence of ≥2 high-risk molecular abnormalities i.e. del17p, t(4;14), t(14;16) or +1q21 (ultra-high risk myeloma) was also more frequent in the EPD group (13.5% vs. 6.6%; $p<0.001$). The percentage of patients treated with lenalidomide-based therapies (LBT), including triplets, did not differ between groups (EPD: 29% vs. others: 33%; $p>0.05$), whereas daratumumab-based therapies (DBT) were administered less frequent in patients with EPD vs. others (2% vs. 10%; $p<0.001$). Autologous stem cell transplantation (ASCT) was given in 11% of patients with EPD vs. 33% of non-EPD ($p<0.001$). Binary logistic regression analysis demonstrated that ISS, R-ISS, R2-ISS, ultra-high-risk myeloma, ASCT and DBT were significant predictors for EPD ($p<0.05$); LBT did not have any prognostic value in the univariate analysis ($p>0.05$). In the multivariate analysis R2-ISS, ASCT and DBT were the stronger significant prognosticators for EPD (HR for R2-ISS: (I) vs. (IV): 0.24; $p<0.001$, (II) vs. (IV): 0.28; $p<0.001$, (III) vs. (IV): 0.48; $p=0.017$), HR for ASCT: 0.26; $p<0.001$, and HR for DBT: 0.18; $p<0.001$). After a median follow up of 77 months (95% CI: 72-83), median progression free survival

and overall survival for patients with EPD vs. others were 10 vs. 40 months ($p<0.001$) and 29 vs.76 months ($p<0.001$), respectively.

Conclusion: In conclusion, >20% of newly diagnosed MM patients experienced EPD, in the real-world setting; EPD patients were more frequently older, with higher tumor burden and high-risk features. Upfront DBT and ASCT were the strongest prognostic factors, reducing by 82% and 74%, respectively the risk for EPD; R2-ISS proved a significant predictor for EPD however, its value was mitigated when adjusted to the type of primary therapies.

O18- SAFETY AND EFFICACY OF BELANTAMAB MAFODOTIN IN COMBINATION WITH LENALIDOMIDE AND DEXAMETHASONE IN PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA WHO ARE INELIGIBLE FOR TRANSPLANT: THE PHASE 1/2 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],Stavros Gkolfinopoulos[2],Kyriaki Manousou[2],Efstathios Kastritis[1],Meletios A. Dimopoulos[1],Evangelos Terpos[1]

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

Objective : The combination of lenalidomide and dexamethasone (Rd) is preferred in the treatment of transplant ineligible (TI) patients (pts) with newly diagnosed multiple myeloma (NDMM). Belantamab mafodotin (belamaf; GSK2857916) is an antibody-drug conjugate targeting BCMA, which has shown efficacy in pretreated MM pts. Preclinical data demonstrate synergy between belamaf and lenalidomide, while these drugs do not have overlapping toxicities. Thus, there is a strong rationale for investigating the belamaf-Rd combination in TI NDMM pts.

Methods : BelaRd (NCT04808037) is an open-label, phase 1/2 study conducted in Greece, aiming to enroll 66 TI NDMM pts. Here we report results from Part 1 which evaluates the safety/tolerability of three belamaf doses (2.5/1.9/1.4 mg/kg) plus Rd in 36 pts and establishes the recommended phase 2 dose (cut-off date 15/04/2023). In this part, belamaf is initially administered q8w and, depending on toxicity, dosing may be rescheduled to q12w.

Results : Of the 36 pts [median age: 72.5 years; male: 19 (53%)] in Part 1, 29 (81%) are still on treatment, while 7 (19%) have discontinued [6 pts due to belamaf-unrelated fatal events: (COVID-19 infection: 1/1/2; Pneumonia: 1/1/0, for cohorts 2.5/1.9/1.4 respectively); 1 pt withdrew consent]. The median belamaf administrations and number of cycles reached were 6/7/7 and 18.5/21.5/18.5, for the respective cohorts. The most common (≥10% of pts) non-ocular ≥ Gr3 treatment-emergent adverse events were fatigue (21 pts, 58%; [7 (58%)/7 (58%)/7 (58%)]), rash (6 pts, 17%; [2 (17%)/2 (17%)/2 (17%)]), diarrhoea (8 pts, 22%; 2 (17%)/3 (25%)/3 (25%)]), insomnia (4 pts, 11%; 0/4 (33%)/0]) and COVID-19 infection (5 pts, 14%; [2 (17%)/1 (8%)/2 (17%)]), while no ≥Gr3 thrombocytopenias and infusion-related reactions were reported. Regarding ≥Gr3 infections other than COVID, pneumonia was reported for 3 (8%) pts [1 (8%)/1 (8%)/1 (8%)]. Among 201/227/192 best corrected visual acuity (BCVA) assessments in cohorts 2.5/1.9/1.4, a worse than 20/50 result (in the better seeing eye) was observed in 21 (10%)/23 (10%)/18 (9%), while BCVA ≤20/200 was noted in 2 (1%)/3 (1%)/11 (6%). The overall response rate was 100% across all cohorts. More specifically, CR or better was achieved in 6 (50%)/4 (33%)/5 (42%), VGPR in 3 (25%)/7 (58%)/4 (33%) and PR in 3 (25%)/1 (8%)/3 (25%) of the pts in cohorts 2.5/1.9/1.4, with a median time to first response of 1 month. Finally, over a median follow-up of 18.7 months no disease progression was observed.

Conclusion: Belamaf-Rd, with the extended schedule for belamaf, has shown a very manageable safety profile with minimal impact in vision-related functioning in an elderly, non-fit pt population. Meanwhile, a very promising clinical activity is observed with rapid, deep and durable responses across all dose levels. Consequently, after validation with bigger pt numbers, this novel combination may well be a very attractive frontline option for this vulnerable TI-NDMM population.

ABSTRACTS
POSTER PRESENTATIONS

P1- BORTEZOMIB THERAPY OF NON-HODGKIN'S LYMPHOMAS: A SINGLE CENTER EXPERIENCE

Kübra Yel Uygun[1],**Atakan Tekinalp**[1],**Sinan Demircioğlu**[1],**Özcan Çeneli**[1]

[1]Necmettin Erbakan University Medicine Faculty Hematology Department

Objective : Some of aggressive non-Hodgkin's Lymphomas (NHL), such activated B cell subtype of diffuse large B cell lymphoma (DLBCL), is characterized by additional signal pathway abnormalities. Activation of NF-kB signal pathway, one of those pathways, demonstrated firstly in plasma cell diseases promotes cell proliferation and inhibits apoptosis. Bortezomib,the first proteazom inhibitor,induces malign cell apoptosis via NF-kB inhibition and also some of caspase-independent mechanisms, and has approved for patient with relapsed mantle cell lymphoma (MCL), one of aggressive lymphomas.

Methods : We analyzed patients undergoing between 01.01.2013 and 01.01.2023 with diagnosed relapse/refractory NHL and received bortezomib based chemotherapy, retrospectively. Kaplan Meier method used to survival analysis.

Results : The study included 14 patients. Of the patients, 8 (57.1%) were male, 6 (42.9%) were female, and the median age was 57 (34-76).All bortezomib based protocols were BORID (Bortezomib, rituximab, dexamethasone). The most common type of NHLs was MCL and included of 10 (71.4%) patients. The others were DLBCL and follicular lymphoma and included of 3 (21.4%) and 1 (7.1%) patient, respectively. The median time from diagnosis to bortezomib for all patients was14,9 months (3-70). Median number of previously therapy was 2 (1-4).Half of the patients with MCL achieved minimum partial response. The median estimated Progression-Free Survival (PFS) and 1-year PFS were 11 months and 36%.

Conclusion: Although bortezomib based regimes was investigated as a first line therapy for active B cell DLBCL, improvement in survival didn't occur in meta-analysis. However, several study including patients with relapsed aggressive lymphomas, particularly MCL, have been shown that overall response rate was about 50%, as in our study.

P2- A CASE OF ACUTE MYELOID LEUKEMIA AFTER LUTETIUM-177 TREATMENT

Selin Kır[1],Ajda Güneş[1],Mine Hekimgil[2],Emin Karaca[3],Fahri Şahin[1],Nur Akad Soyer[1],Güray Saydam[1]

[1]Ege University Faculty of Medicine,Department of Hematology, [2]Ege University Faculty of Medicine, Department of Pathology, Izmir, Turkey, [3]Ege University Faculty of Medicine, Department of Medical Genetic

Objective : Introduction: The incidence of neuroendocrine tumors is increasing worldwide. In 2018, Lutetium-177 received FDA approval for the treatment of NETs.Side effects associated with this treatment include myelotoxicity and nephrotoxicity due to reabsorption of radiopeptides, accumulation in the renal interstitium. According to a previous systematic review and meta-analysis, myelodysplastic syndrome and acute myeloid leukemia were not observed after the use of Lutetium-177. Herein,. We aimed to present a case of acute myeloid leukemia after the use of Lutetium-177.

Methods : Aims: The side effects of new agents used in the treatment of oncologic and hematologic malignancies should be well known, side effects such as myelotoxicity should be kept in mind, and the patient should be consulted to hematology in case of unexplained cytopenia for potential MDS and acute leukemia.

Results : Case: A 56-year-old female patient underwent right hemicolectomy in 2018, the pathology result revealed well-differentiated neuroendocrine tumor, and she was followed up for 3 years without treatment. She received 6 doses of lutetium treatment in nuclear medicine due to the development of liver and pleural metastasis during follow-up. Later on, the treatment was continued with 6 doses of subcutaneous octreotide injection. She was consulted to hematology because of weakness, easy bruising and bleeding gums and pancytopenia in follow-up examinations. Laboratory values at the time of admission: WBC: 2.98 X 10^3/µL, neutrophil: 0.24x 10^3/µL, platelet: 47 x 10^3/µL, hemoglobin: 9.4 x g/dL, sedimentation: 118 , CRP: 150 mg/L renal and liver functions were normal. Peripheral smear showed 20-30% blastic cells. Bone marrow biopsy was consistent with acute myeloid leukemia. Approximately 90% of the cells in the bone marrow aspiration smear and imprint preparation had blastic morphology with aberrant TdT expression as well as CD34, CD68-KP-1, CD117 and MPO in blastic cells. Chemotehrapy containing Idarubicin, Cytarabine was started. Venetoclax at a dose of 100 mg was added due to confirmation of translocation in the CBFB gene at the 16q22 locus with a rate of 90%.Possibly related to t(16;16)(p13.1;q22) or inv(16)(p13;q22) in FISH analysis. . Control bone marrow biopsy performed after first cycle of this treatment confirmed remission with hypocellular (10%) bone marrow without any blastic cells. The patient was planned to receive venetoclax and azacitidine as consolidation treatment and continues to follow-up in our clinic.

Conclusion: Conclusion: Lutetium-177 is a relatively newly used agent in the treatment of neuroendocrine tumors. Myelosuppression is among its side effects. In patients receiving this treatment, hemograms should be monitored at regular intervals and in case of cytopenia, the patient should be referred to hematology without losing time. Until to date, there is only one case of chronic myeloid leukemia in the literature and our case, based on our search, is the first case of acute myeloid leukemia in the literature. It should be kept in mind that cytopenias that develop after oncologic treatments may be caused by other hematologic malignancies.

P3- "SINGLE-CENTERED REVIEW OF BACTERIAL INFECTIONS IN PATIENTS WITH NEUTROPENIC FEVER WHO RECEIVED CHEMOTHERAPY IN HEMATOLOGY CLINIC OF EGE UNIVERSITY HOSPITAL BETWEEN JANUARY 2017- DECEMBER 2019" RETROSPECTIVE OBSERVATIONAL STUDY.

Bora Comert[1],Nigar Abdullayeva[2],Nur Soyer[2],Guray Saydam[2]

[1]Department of Hematology, University of Health Sciences, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey, [2]Department of Hematology, Ege University Hospital Izmir, Turkey

Objective : Febrile neutropenia (FEN) occurs during and after chemotherapy (CT) applied in patients with hematological malignancies. FEN-related mortality rates are quite high. Our study discusses FEN diagnosis methods, risk assessments, agents in patients with bacterial infections, empirical and broad-spectrum treatments for these agents, conditions affecting the treatment process, and adverse outcomes.

Methods : The study included 193 patients (mean age 50 years and 51.8% women) who received chemotherapy and developed neutropenia in Ege University Hospital Hematology Clinic between January 2017 and December 2019 from the electronic database. Patients under the age of 18, patients who received allogenic bone marrow transplantation, patients with FEN who developed bacterial infection without CT, and patients with hematological malignancies whose bacterial focus and causative agent were not determined even though they received multiple antibacterial treatments were not included in the study.

Results : In the study, a significant correlation was found between mortality and diagnosis (p=0.033), disease phase (p=0.033), and granulocyte colony-stimulating factor (G-CSF) administration (p=0.002). It was found that mortality was higher in those who were not administered G-CSF compared to those who were administered, and the mortality rate was higher in those diagnosed with leukemia and in the remission induction phase. There was a statistically significant correlation between the mortality and the duration of neutropenia (p= 0.028), the c-reactive protein (CRP) level at the start of chemotherapy (p= 0.005), the day on which neutropenia was reproduced (p=0.001), the time to neutropenia (p=0.001). According to this, mortality was higher in those with a long period of neutropenia, with a high CRP when chemotherapy was started, and with a longer period of neutropenia and bacterial growth.

Conclusion: Early recognition of infections and effective empirical antibiotic therapy is important in febrile neutropenic patients. In this context, the determination of the flora of a center, common infections, parameters that may help the diagnosis, and its effectiveness are guiding. At the same time, it is thought that the identification of the primary risk factors that may be effective in neutropenic fever and mortality will contribute to the determination of the empirical treatment protocols of the patients.

P4- A RETROSPECTIVE ANALYSIS OF ACUTE PROMYELOCYTIC LEUKEMIA; A SINGLE CENTER EXPERIENCE

Hale Bülbül[1],Alper Togay[2],Fatma Keklik Karadağ[1],Aybüke Olgun[1],Cengiz Ceylan[1]

[1]Department of Hematology, University of Health Sciences, Tepecik Training and Research Hospital, İzmir, Turkey, [2]Department of Medical Microbiology, University of Health Sciences, Tepecik Training and Research Hospital, İzmir, Turkey

Objective : Acute myeloid leukemia (AML) is,in itself, a rare disease. Acute promyelocytic leukemia (APL) is a particularly aggressive subtype of AML and accounts for approximately 10% of AML cases. Large studies have shown the median age of 33 and 40 years. The incidence did not vary by gender. APL represents a medical emergency with a high early mortality rate. This is evidenced by the fact that the early mortality rate in patients participating in clinical trials is less than 10%, whereas the early mortality rate in the general population is still more than 15%. Data on APL patients from Türkiye are limited. Therefore, we aimed to determine the clinical features, FLT3 mutation status and survival outcomes of patients with APL who were diagnosed in our center in the last 5 years.

Methods : 15 patients diagnosed with APL between 2017 and 2022 were retrospectively analyzed. Survival analysis was performed using Kaplan-Meier analysis

Results : The mean age was 56.5±15.7 years with a median of 61 years. The female-to-male ratio was 1.5:1. The majority of our patients had the hypergranular variant (73.3%). Risk stratification revealed that low-risk disease predominated (93.3%). Bleeding and thrombosis occurred in 40% and 13.3% of patients, respectively. 13.3% of patients died due to early hemorrhagic complications with disseminated intravascular coagulation. Overall, 10 (66.6%) patients survived, and 5 patients (33.3%) died. 3 patients died within 2 days after diagnosis. The early mortality rate was 20%. 5 (33.3%), 1 (6.6%) and 6 (40%) patients were treated with all-trans retinoic acid + arsenic trioxide (ATRA+ATO), ATRA+Idarubicin and 7+3 regimene+ATRA, respectively. The rate of complete remission was 100%. Median event-free survival (EFS) and overall survival (OS) were not reached, whereas the median of EFS and OS were 34.1 and 37 months, respectively. The 1-year OS rate was 66.7%. FLT3 mutation status was known in 8 patients. FLT3- ITD and TKD mutations were found in 2 and 3 patients, respectively. No FLT 3 mutation was observed in 3 of 8 patients. 1 of 2 (50%) patients who had FLT3-ITD and 1 of 3 (33.3%) patients who had FLT3-TKD mutations were died.

Conclusion: Most of our cohort consisted of female patients with advanced age and low risk disease and this study shows that early death is now the greatest factor in treatment failure for this otherwise curable form of leukemia. Despite the low early mortality rates in clinical studies, it should be kept in mind that early mortality may be higher in reality. In this study, the high molecular CR rate was found to be independent of remission induction therapy for APL. There are limited data showing an association between the FLT3- ITD mutation and decreased OS. The clinical significance of FLT3 ITD mutation in patients with APL remains controversial. Conversely, FLT3-TKD mutation has not been associated with the hematologic features of APL and studies show no correlation between FLT3-TKD mutation and disease outcome. Further studies with larger numbers of patients are needed to confirm the above-mentioned findings.

P5- A RARE PRESENTATION OT T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA IN THE PREVIOUSLY KNOWN AS CHRONIC LYMPHOCYTIC LEUKEMIA

Bahar Sevgili[1],Damla Çağla Patır[1],Ajda Güneş[1],Güray Saydam[1],Mine Hekimgil[2],Derya Demir[2],Filiz Vural[1]

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

Objective : Richter's transformation (RT) is a rare complication of chronic lymphocytic leukemia (CLL) or low-grade lymphoma sudden onset of clinical deterioration and signs of accelerated tumor burden. Transformation to large cell lymphoma (diffuse large B-cell lymphoma, etc.) and Hodgkin's disease (HH) has been mostly reported in patients. In our case, We aimed to present the case report of T-cell acute lymphoblastic leukemia (T-ALL) as a result of investigations performed with a differential diagnosis of RT.

Methods : A 61-year-old male patient with known hypertension was admitted to our center in 2014 with a diagnosis of CLL who had been investigated for diffuse lymphadenopathy (LAP) and constitutional symptoms. Cytogenetic analysis by fluorescence in situ hybridization (FISH) revealed no 17p deletion, IgH, 11q deletion or 13q deletion. The patient, who was evaluated as RAI stage 3 at the time of diagnosis, was considered in remission after R-FC chemoimmunotherapy protocol was applied in the 1st step treatment.6 years later, due to the development of B symptoms and diffuse LAPs, 3 cycles of R-FC protocol was administered again but he could not end up his treatment as his follow-up was interrupted for 1.5 years due to the Covid-19 pandemic. In 2021, bone marrow aspiration and biopsy (BMAB) was performed due to stage 3 CLL/. No mutation was detected in the karyotype and cytogenetic analysis by FISH in the patient who was diagnosed with CLL as a result of BMAB. During the 17th cycle of ibrutinib 420 mg/g as 3rd line treatment, the patient was evaluated for darkening in urine and B symptoms. His laboratory results resulted as leukocyte :2100/µl, lymphocyte 480/µl, hemoglobin: 6,1 g/dl, platelets: 48000/µl, uric acid: 13,5 mg/dl and potassium: 5,5 meq/l. Whole body computed tomography (WBCT) revealed massive hepatosplenomegaly and LAPs in the abdomen, the largest of which was 53x50 mm. The patient was admitted to our service with a pre-diagnosis of RT/secondary malignancy.

Results : In the aspiration smear of the patient who underwent BMAB showed a diffuse lymphoblastic cell population infiltrating 80% of the bone marrow and increased reticular fiber grade III. Immunohistochemical examination revealed positive CD2, CD3, CD7, GATA3 and ki-67 proliferation index was 100% in neoplastic cells.CD4, CD8, CD5, CD1a, CD33, CD34, TdT, CD79a, TCR beta/gamma and delta were negative. FISH did not detect 17p del, IgH, 11q, 13d del. Conventional cytogenetic analysis revealed 45,X,-Y(2). In the light of all findings, HyperCVAD chemotherapy protocol was planned considering T-ALL in the foreground. After 2 cycles of HyperCVAD A+B protocol, allogeneic stem cell transplantation from an unrelated donor was planned in the 1st remission and the pre-transplant preparation process continues in our center.

Conclusion: RT cases are an emergency picture characterized by progressive clinical deterioration in cases of low-grade leukemia/lymphoma. It is known that the majority of CLL cases transform into large B-cell lymphoma, while Hodgkin lymphoma develops less frequently.1 In a patient with known CLL background, newly developing acute lymphoblastic leukemia of T-cell origin may be considered among the differential diagnoses in collaboration with hematology and pathology.

P6- EXTRALYMPHATIC INVOLVEMENT AND BONE INVOLVEMENT ARE A FACTOR ON RELAPSE/PROGRESSION IN NON-HODGKIN LYMPHOMA?

Ayşe Uysal[1],Mustafa Merter[1]

[1]Fırat University School of Medicine Hematology Department

Objective : In this retrospective study, we aimed to examine the effect of extralymphatic involvement, bone involvement and then number of areas with extralymphatic involvement on relapse/progression in patients with non-Hodgkin lymphoma (NHL).

Methods : In this study, 165 patients followed in the Hematology clinic of Fırat University Hospital between 2004-2022 were evaluated retrospectively. Demographic and clinical data of the patients, presence of extralymphatic disease, bone involvement, relapse rate and event-free survival (EFS) were evaluated.

Results : A total of 165 (63.5%) patients were diagnosed with NHL. The median age at the time of diagnosis was 61 years (20-91) and 90 (54.5%) of them male. Extralymphatic involvement was detected in 69 (41.8%) of all patients at the time of diagnosis. Fifteen (9.1%) of them with extralymphatic involvement had extralymphatic involvement in more than one area. Bone involvement was the most common (n: 21, 36.4%) extralymphatic involvement, followed by stomach (n: 16, 23.2%) and bone marrow (n:12, 17.4%) involvement, respectively. In the median follow-up time was 40 (range, 1-161) months, the relapse was detected in 18 (10.9%) patients and 10 (55.5%) of them had extralymphatic involvement at the time of diagnosis. The mean EFS time was 88.35 (95% CI 78.8-97.89) months and 134.16 (95% CI 114.72- 153.59) months in patients with extralymphatic involvement and in patients without extralymphatic involvement, respectively. EFS detected shorter in patients with extralymphatic involvement than in patients without extralymphatic but there was no statistically significant difference between the extralymphatic involvement and without extralymphatic involvement (p=.186). The mean EFS was 91.9 (95% CI 78.2-105.7) months in patients with bone involvement and 81 (95% CI 70.2-91.9) months in patients with extralymphatic involvement other than bone involvement. There was no statistically significant difference between the bone marrow involvement and extralymphatic involvement other than bone involvement and without extralymphatic involvement (p=0.220). When the EFS is evaluated in patients with more than one extralymphatic involvement, the median EFS was 85.33 (95% CI 69.02-101.65) months, while 126.6 (95% CI 109.36-143.85) months in patients with 1 or less extralymphatic involvement. There was no statistically significant effect of the number of extralymphatic involvement on EFS (p=0.776).

Conclusion: In our study, extralymphatic involvement, bone involvement, and the number of areas with extralymphatic involvement had no effect on relapse/progression.

P7- AN UNUSUAL JAK INACTIVATION WITH PREVIOUSLY KNOWN THROMBOCYTOPENIA, AND NEWLY DIAGNOSED B CELL ACUTE LYMPHOBLASTIC LEUKEMIA: A DISCUSSION FOR POTENTIAL EFFECTS ON BASIS AND PROGNOSIS OF B-ALL MANAGEMENT

Bahar Sevgili[1],Ajda Güneş[1],Derya Demir[2],Nazan Özsan[2],Güray Saydam[1],Fahri Şahin[1]

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

Objective : Genomic profile of Philadelphia chromosome negative (Ph-) B cell acute lymphoblastic leukemia (B-ALL) mainly consists of recurrent genetic abnormalties (hypo or hyperdiploidy), translocations of fusions of thyrosine kinase receptors. Germline mutations that cause inactivation of janus kinase receptors (JAK) is associated with bone marrow failure and premature death in mice. Somatic mutations that cause JAK inactivation in bone marrow is not well understood yet. Increased PD-L1 resistance has been noted in colon cancer and melanoma case series with JAK inactivation mutations. Here we aimed to present a case report of B-ALL with JAK inactivation and potential effect on clinical progress.

Methods : A 68-year-old male patient with known hypertension. While he had been followed up in an external center since 2018 due to thrombocytopenia, he was referred to our center in June 2022 due to weight loss and monocytosis. On physical examination, general condition was good, vitals were stable, neurologic, respiratory, and cardiovascular system examinations were normal. No hepatosplenomegaly or pathologic lymphadenopathy was found. Complete blood count showed leukocytes: 29080/µl, lymphocytes: 3430/µl, monocytes: 7350/µl and 2% blasts in the peripheral smear, bone marrow aspiration and biopsy (BMAB) revealed B-ALL. No mutation was detected in conventional cytogenetic analysis and HyperCVAD chemotherapy (CT) protocol was initiated. After the 1st induction CT, septic shock and prolonged thrombocytopenia were detected, and the 2nd CT protocol was administered with a dose reduction. Allogeneic stem cell transplantation ("AlloSCT") from a fully matched sibling donor (MSD) was planned for the patient who was in remission after induction CT.

Results : During the preparations for transplantation, monocytosis and thrombocytopenia persisted, and a BMAB revealed increased blasts and mildly increased myeloid precursors. Next generation sequencing (NGS) analysis revealed JAK2 p.I437 inactivation with frameshift mutation. AlloSCT from MSD was performed on June 23 while the patient was in remission after salvage KT and no new pathology was detected in conventional cytogenetic analysis. Posttransplant follow up is under remission.

Conclusion: JAK2 V617F mutation is mostly determined in myeloproliferative neoplasms (MPN) and rarely myelodysplastic neoplasms/ myeloproliferative neoplasms (MDN/MPN) with ring sideroblasts and thrombocytosis. Other JAK mutations in hematologic malignancies have not been described well, nevertheless potential effects on survival are not known yet. We would like to perform NGS analysis to determine any overlap chronic myelomonocytic leukemia (CMML) /MDN or MDN/MDN overlap syndromes. Neither cytomorphologic appearance nor cytogenetic analysis reveal any sign of clonal monocytic or proliferative disorder. On the other hand, previous history of mild thrombocytopenia and development of B-ALL, JAK2 inactivation we detected with NGS could be a sign of myelodysplastic baseline. There are limited data on JAK inactivation and bone marrow effect. We would like to present clinical follow-up and we aimed to contribute to the literature to improve our knowledge about JAK mutations. In conclusion, we need more randomized clinical trials to better understand the potential effects of JAK inactivation significantly.

P8- PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA: RETROSPECTIVE ANALYSIS OF 19 CASES IN A SINGLE CENTRE

Denis Bozer[1],Ajda Güneş[1],Derya Demir[2],Serra Kamer[3],Nur Akad Soyer[1],Fahri Şahin[1],Filiz Vural[1],Mahmut Töbü[1],Güray Saydam[1]

[1]Ege University Faculty of Medicine, Department of Hematology, İzmir, [2]Ege University Faculty of Medicine, Department of Pathology, İzmir, [3]Ege University Faculty of Medicine, Department of Radiation Oncology, İzmir

Objective : Primary central nervous system lymphoma (PCNSL) is a rare and aggressive non-Hodgkin lymphoma that affects the brain, eyes, cerebrospinal fluid (CSF), or spinal cord without systemic involvement and approximately 90% of PCNSL cases are diffuse large B- cell lymphomas (DLBCL). Current treatments of PCNSL are a high-dose methotrexate (HD- MTX) -based polychemotherapy and whole-brain radiotherapy.

Methods : Patients who were treated with the high dose methotrexate based regimen ± whole brain RT in our hematology department between 2012 and 2021 were analyzed retrospectively. All the patients with PCNSL were histologically documented with the examination of mass biopsy materials or surgically resected specimens. Contrast-enhanced computed tomography (CT), positron emisssion tomography (PET) and bone marrow biopsy was performed to confirm the absence of systemic disease.

Results : Total nineteen cases are retrospictevely evaluated. Median follow-up was 9,63±4,2 months and median age was 47 years (range 18–81). Two of the cases of PCNSL were associated with renal transplantation, 1 case was associated with HIV infection. The Ki67 index in all patients was evaluated as >70%. Thirteen patients had received 2 cycle R- IDARAM, 2 patient had recieved MATRIX, 3 patients had received 2 cycles of HD-MTX monotherapy, 1 patient had recieved rituksimab monotherapy due to age. Twelve patient had chemotherapy followed by WBRT. Seven patients received ASCT as second line treatment, the first line treatment of these patients were given R-IDARAM protocol. The median overall survival is 9,63±4,2 months, the median progression-free follow-up was 8.9 months. Responses to first line treatments had been complete remissions (CR) in 9 (40%) patients, partial remissions (PR) in 6 (40%) patients, respectively. Four patients died during the course of chemotherapy. The median overall survival of patients who received chemotherapy followed by WBRT was 77.3±31.5 months, and the positive effect of WBRT on survival was observed. (p: 0,019 hazard ratio 0,11 (95%CI 0,01- 0,6)). No significant effect was found on survival with ASCT following cehmeoterap with or without WBRT (p:0,282).

Conclusion: Primary central nervous system lymphomas are rare and have poor prognosis. A significant difference was observed in terms of survival in patients who received chemotherapy and radiotherapy. Further clinical trials with a larger number of patients are required to evaluate appropriate treatment options for prolonging the life expectancy of patients.

P9- MULTIPLE MYELOMA IN A PATIENT WITH CHRONIC MYELOID LEUKEMIA: A CASE REPORT

Selin Kır[1],Nazan Özsan[2],Emin Karaca[3],Nur Akad Soyer[4],Fahri Şahin[5],Güray Saydam[6]

[1]Ege Üniversitesi Tıp Fakültesi, İzmir

Objective : Chronic myeloid leukemia (CML) is a disease characterized by clonal proliferation of pluripotent hematopoietic stem cells resulting from Philadelphia chromosome positivity.Multiple myeloma (MM) is a disorder of uncontrolled proliferation of plasma cells derived from a single clone,characterized by renal failure,lytic bone lesions,hypercalcemia and anemia.Synchronous or metachronous presentation of MM and CML in the same patient is extremely rare.To date,a limited number of cases of MM associated with CML have been reported and the reason behind the co-occurrence of both malignancies is not understood.Here, we report a case of a patient diagnosed with CML who developed MM 16 years later.

Methods : In case of treatment non-response in CML,bone marrow biopsy should be performed to investigate the presence of other hematologic malignancies.It should be kept in mind that multiple hematologic malignancies may be seen in the same patient at the same or different times.

Results : A 71-year-old female patient was diagnosed with CML at an external center, followed up under imatinib treatment, and switched to nilotinib treatment due to loss of molecular response. She was switched to dasatinib treatment due to severe nausea and vomiting complaints under nilotinib treatment.She developed shortness of breath and bilateral massive pleural effusion was detected on chest radiography. After excluding cardiac and other causes of pleural effusion,it was thought to be dasatinib-related and dasatinib treatment was discontinued. The patient voluntarily discontinued treatment for 3 months. The patient referred to our clinic due to loss of hematologic response and ponatinib 45 mg/day was started by us. Under ponatinib treatment, ponatinib treatment was discontinued due to skin peeling, anemia and thrombocytopenia.Under the current treatment, bcr abl (p 210) IS: 74.96% and t (9:22): 94.06% were measured, WBC: 23.2 x 10^3/µL, neutrophil: 14.5 x 10^3/µL, monocyte: 4.78 x 10^3/µL, hgb: 13.5 x g/dL, plt: 142 x 10^3/µL. No blastic cell was observed in peripheral smear. Bone marrow biopsy showed increased plasma cells in dense interstitial distribution forming groups with CD138 up to 40%, most of the plasma cells were positive with kappa and a few with lambda and multiple myeloma was diagnosed. VCD chemotherapy was started.

Conclusion: ML is a myeloproliferative disorder characterized by the proliferation of pluripotent hematopoietic stem cells.MM is characterized by abnormal proliferation of plasma cells differentiated from lymphoid B cells. Therefore, the abnormal cell types of CML and MM are markedly different.The mechanism of synchronous or metachronous occurrence of these two malignant tumors in the same patient is not fully understood.Different hypotheses have been proposed about this issue.One of them is that MM occurs as a consequence of CML treatment.Another potential hypothesis is that multiple myeloma and CML share the presence of malignant pluripotent progenitor stem cells.This suggests the ability of CML to differentiate into either myeloid or lymphoid cells.The third hypothesis is the presence of host-specific factors,which also explain the presence of two different malignancies in the same host.Pre-existing CML may create a more sustainable environment for the formation of secondary malignancies.As there are multiple hypotheses,more cases are needed to further investigate and monitor potential related conditions.

P10- A CASE OF TONSILLAR AMYLOIDOSIS

Ali Yılmazer[1],Ajda Güneş[1],Nur Soyer[1],Güray Saydam[1],Ali Veral[2],Sait Şen[2],Serra Kamer Arun[3]

[1]Department of Hematology, Ege University Medical Faculty Hospital, Izmir, Turkey, [2]Department of Pathology, Ege University Medical Faculty Hospital, Izmir, Turkey, [3]Department of Radiation Oncology, Ege University Medical Faculty Hospital, Izmir, Turkey

Objective : A 56-year-old female patient had bilateral mastectomy due to breast cancer in 2022. The patient, who did not have a history of chemotherapy, was under follow-up with hormonal therapy. The biopsy was taken because of a mass in the oropharynx by the otolaryngologist, whom she went to due to sore throat, and it was concluded as amyloidosis (non-AA type). Lambda light chain and serum amyloid A levels were found to be slightly elevated in the examinations of the patient, who was referred to the hematology department for further examination. In the serum immunofixation electrophoresis of the patient whose immunoglobulin values were normal, paraproteinemia was not detected. Bone marrow biopsy was normocellular. No involvement outside the oropharynx was observed in the simultaneous PET/CT of the patient. A tonsil biopsy of the patient resulted in amyloidosis. The patient, whose creatinine and urine protein values were normal, and no cardiac involvement was detected, was evaluated as isolated tonsillar amyloidosis and was interviewed in terms of radiation oncology and radiotherapy. The decision to follow up was given to the patient who did not have any active complaints.

Methods :

Results :

Conclusion: Amyloidosis is an accumulation of an abnormal protein with eosinophilic fibrillary structure in the intercellular space of different tissues and organs because of different causes. It may be systemic or localized, primary or secondary. Amyloidosis is rarely seen in the oral cavity. In this case, we wanted to share our clinical experience.

P11- COEXISTENCE OF BLASTIC PLASMOCYTIC DENDRITIC CELL NEOPLASIA, ACUTE MYELOID LEUKEMIA AND LUNG CANCER

Ali Yılmazer[1],Nigar Abdullayeva[1],Ajda Güneş[1],Nur Soyer[1],Güray Saydam[1],Nazan Özsan[2]

[1]Department of Hematology, Ege University Medical Faculty Hospital, Izmir, Turkey, [2]Department of Pathology, Ege University Medical Faculty Hospital, Izmir, Turkey

Objective :

Methods :

Results : A 63-year-old male patient with known comorbidity of hypertension was referred to us because of blastic plasmacytic dendritic cell neoplasia (BPDCN) as a result of the biopsy taken in the dermatology outpatient clinic, where he applied for atrophic skin lesions with erythematous follicular prominence, starting from the lumbar region and spreading to the back and anterior chest wall. In the initial evaluation of the patient, thrombocytopenia and leukopenia were present, while myeloid precursors and blasts were observed in the peripheral blood smear. On the thoracoabdominal CT, a 24x21 mm nodule in the left lung apex in favor of primary lung malignancy with a spiculated edge, a 5x5x5 cm solid mass lesion in the left adrenal gland, and numerous pathological lymph nodes in the abdomen and axilla were seen. Due to the patient's primary diagnosis and peripheral smear findings, bone marrow biopsy was performed. Simultaneously, a biopsy was planned to elucidate the lesion in the lung. In the bone marrow biopsy of the patient, acute myeloid leukemia was diagnosed, and when evaluated with immunohistochemical examinations, CD34 and CD117 and positive blastic cells were detected around the trabeculae at a rate of 20%, İn the middle of this cell population, CD123, TCL1, CD56, CD4 and CD43 Positive cell population was seen showing the plasmacytic dendritic cell phenotype. In the transthoracic fine-needle aspiration biopsy performed for the mass in the lung, the patient was diagnosed with non-small cell lung carcinoma, and the subtyping could not be performed precisely because the biopsy material was insufficient. Tru-cut biopsy performed from the lymph node in the axilla to determine the type of lung malignancy of the patient resulted in BPDCN. In the light of this information, the patient's treatment was started as 7+3 chemotherapy. After chemotherapy, the patient's skin lesions regressed. Bone marrow biopsy performed as a control was evaluated as normocellular. In the imaging taken for lung malignancy, the lesion in the lung remained stable, while the metastasis in the left adrenal gland was observed to have progressed. In the light of this information, a treatment plan was drawn up for the patient by ESHAP chemotherapy increasing the day with cytarabine and venetoclax po. While the patient's cytopenias improved after the treatment, the skin lesions at the time of first diagnosis started to reappear. Progression was observed in the axillary lymph node, which also had a diagnosis of BPDHN. Tagraxofusp was applied to the patient whose control bone marrow biopsy was evaluated as normocellular. The follow-up and treatment of the patient continues.

Conclusion: Blastic plasmacytic dendritic cell neoplasia is a rare, malignant tumor that has been described in recent years. The diagnosis is usually made by applying the appropriate immunohistochemistry panel in the skin biopsy. There is no consensus on treatment and life expectancy is short. In our patient, the presence of AML and lung malignancy together with the diagnosis of BPDHN complicates us in terms of treatment. With this article, we wanted to share our patient-specific experience with you.

P12- ACUTE RENAL FAILURE SECONDARY TO CHRONIC LYMPHOCYTIC LEUKEMIA: A CASE REPORT

Nigar Abdullayeva[1],**Fatma Keklik Karadag**[2],**Mine Hekimgil**[3],**Guray Saydam**[1]

[1]Department of Hematology, Ege University Hospital Izmir, Turkey, [2]Department of Hematology Tepecik Training and Research Hospital Izmir, Turkey, [3]Department of Pathology Ege University Hospital Izmir, Turkey

Objective : Acute renal failure (ARF) secondary to chronic lymphocytic leukemia (CLL) has several causes. An extremely rare cause of renal dysfunction is extensive leukemic infiltration in the renal interstitium. This diagnosis should always be considered when a patient with CLL presents with renal failure, regardless of the clinical stage. In this case, a CLL patient who developed acute renal failure secondary to massive leukemic infiltration of the kidney and was treated with chemotherapy and had a significant improvement in renal function is presented.

Methods : A 62-year-old male patient was diagnosed with CLL in July 2018 as a result of a left cervical lymph node (LN) excisional biopsy. The patient, who was followed up with stage I disease without treatment, was admitted to our clinic in November 2019 with ARF. The patient, who had a history of operation and postoperative radiotherapy for colon cancer in 1991, has been followed up with colostomy since then. A renal biopsy was performed to investigate the etiology of ARF in the patient with no known history of renal pathology and normal renal function tests, and the pathology result was CLL infiltration (Ig G, A, M, kappa, and lambda negative, CD5, CD20, CD23 diffuse positive). CLL infiltration (CD20+, CD5+, CD23+) was observed in the bone marrow aspiration biopsy (BMAB) performed on the patient who also had deep anemia. As a result of the positron emission tomography (PET) performed on the patient for staging purposes, the spleen and liver were normal in size, multiple LNs in the cervical, thoracic, and abdominopelvic areas, the posterior wall of the nasopharynx and bilateral tonsillar area were observed to be hyperplasic, hypermetabolic, and were reported to be consistent with CLL involvement. Stage IV disease was accepted, and the patient was given 6 cycles of R-CVP (Rituximab, Cyclophosphamide, Vincristine, Prednisolone) chemotherapy regimen. The laboratory results of the patient who needed hemodialysis 5 times during the hospitalization, before the treatment, on the 15th day, and the 1st month are shown in the table. The patient, whose treatment was completed in May 2020, was followed by normocellular BMAB results. The patient was followed up in remission without treatment for 3 years and developed B symptoms and diffuse lymphadenopathy in March 2023. LN excisional biopsy was performed from the right inguinal region, and it resulted in CD 5 Negative CLL. In the cytogenetic result sent from the peripheral blood, 18% deletion was detected in the 17p13 locus TP53 gene. The patient was evaluated as relapsed CLL and was started on Bruton's tyrosine kinase inhibitor (BTK) Ibrutinib, a second-line treatment. The patient's B symptoms regressed, his anemia improved, and his lymph nodes remained stable. The patient's follow-up and treatment continue.

Results : Lab results across Clinical Courses Leuko/Lympho 10^3/µL Hgb g/dL PLT 10^3/µL Urea/cre mg/dL Glob g/dL Moment of Diagnosis 13.09/6.79 11.2 290 39/0.99 8.1 At Hospital Admission 12.49/6.47 7.6 188 97/8.24 88.7 After R-CVP 15th day 10.73/4.2 6.7 382 159/4.53 54.6 in the 1st month 8.43/2.99 7.9 445 181/2.35 58.1 Before ibrutinib 5.96/1.98 8.8 236 72/2.47 49 Current 13.98/7.49 10.1 239 67/1.87 48.4

Conclusion: Leukemic infiltration causing acute renal failure in CLL is an extremely rare condition. However, it should be considered in the differential diagnosis as it responds very well to various CLL treatments.

P13- A CASE WITH CYCLIC THROMBOCYTOPENIA

Fatma Keklik Karadag[1],Ajda Gunes[2],Nihal Mete Gokmen[3],Fahri Sahin[2],Guray Saydam[2]

[1]Tepecik Research and Training Hospital,Department of Hematology, Izmir, Turkey, [2]Ege University Department of Hematology, Izmir, Turkey, [3]Ege University Department of Allergy and Immunology, Izmir, Turkey

Objective : Cyclic thrombocytopenia (CTP) is a very rare condition and periodic fluctuation of the platelet count is mandatory for the diagnosis. The pathogenesis of CTP is unclear and most likely heterogeneous however, usually there is no clue for the underlying disease. Unfortunately, most of CTP patients are misdiagnosed as primary immune thrombocytopenia (ITP).

Methods : We describe a case with CTP.

Results : Our patient is a 50-year-old female with no medical history but she has a past surgical history significant for thyroid lobectomy. She presented to the hospital for further management after she was found to have a low platelet count of 21 x 10^9/L (range: 150-450 x10^9/L) on her routine examination. On further history, she reported petechiae in her extremities some times. There was no organomegaly or lymphadenopathy and cytopenia other than thrombocytopenia. On further review of laboratory workup in the past several years, she was noted to have multiple episodes of low platelet counts. We performed CBC every week for 3 months and saw the recurrent pattern of fluctuations in her platelet count with improvements sometimes without intervention. No infiltration was detected in bone marrow aspiration and biopsy. Based on and periodic fluctuation of the platelet count she was diagnosed with CTP.

Conclusion: CTP is a rare disease but it should be considered for ITP patients who did not respond standard therapy. It was reported to be related with thyroid diseases, menstruation cycle and some infections such as hepatitis B. Currently, there is no known etiology for CTP and no guidelines for the treatment of CTP yet.

P14- REAL-LIFE EXPERIENCE WITH POMALIDOMIDE PLUS DEXAMETHASONE IN PATIENTS WITH MULTIPLE MYELOMA: A SINGLE CENTER RETROSPECTIVE STUDY

Betül Kübra Tüzün[1],Zühal Demirci[1],Gülçin Çelebi[2],Ajda Güneş[1],Derya Demir[3],Nur Soyer[1],Fahri Şahin[1],Mahmut Töbü[1],Filiz Vural[1],Güray Saydam[1]

[1]Ege University School of Medicine, Department of Hematology, [2]Ege University School of Medicine, Department of Internal Medicine, [3]Ege University School of Medicine, Department of Pathology

Objective : Multiple myeloma (MM) is a heterogeneous disease with the uncontrolled clonal proliferation of plasma cells, accounting for approximately 10% of all hematologic cancers .Hence without curative therapy, the treatment aims to improve overall survival. Pomalidomide (POM) is a third-generation immunomodulatory agent. It has an proapoptotic and antiproliferative action on tumor cells.We retrospectively analysed all patients treated with pomalidomide at our centre between 2017 and 2023.

Methods : All patients who had received or were currently receiving treatment with pomalidomide at Ege University Hematology Outpatient Clinic between January 2017 and August 2023 were included.

Results : A total of 25 patients who received treatment with pomalidomide were identified. Of these, 24 were able to be included in response analyses. Of the remaining 1 patient for whom response could not be assessed ,had an anaphylactoid reaction with pomalidomide and did not complete a single cycle of treatment. Median patient age at diagnosis was 55 years (range 42–82), 7 (28%) patients were 65 or older than 65 years old. 13 patients were male (54,25%) and 11 were female (45,85%). .Nearly all patients had received at least two previous lines of therapy and, as per guideline, had been exposed both to lenalidomide and bortezomib. Efficacy In a total of 24 patients, the treatment response rate (ORR), including all patients with a partial response or better, was 41.7%. A total of 10 patients gained a partial response (3) or a complete response (7). Median progression-free survival (PFS) was were 18,95 ±5,18 months. Median (IQR) treatment duration was 8 (2-47)months. 2 years OS had adjusted as 35,4 ±12,8 % .The most common adverse events were hematologic toxic effects , such as neutropenia (11 patients), anemia (3), thrombocytopenia (1); we also described gastrointestinal symptoms such as diarrhea, infections or sepsis, pneumonia.

Conclusion: In this study, we analyzed the efficacy of oral pomalidomide plus dexamethasone regimen in our patients that received more than one cycle of POM-DEX therapy. Although our patients received POM-DEX at an advanced stage of disease the findings from our real-life experience indicate that Poma-D is a safe and well-tolerated regimen with acceptable toxicity. The ORR reported in our study was 41.7% and is better than previous studies (33% in MM-002, 31% in Nimbus, and 32.6% in Stratus). The PFS observed in our cases of 18,95 ±5,18 months is also quite favorably comparable with that of previously mentioned trials (which described median results of 4.0–4.6 months). Nowadays triplet regimens are widely considered the standard of care in myeloma. Though the efficacy of POM-DEX, should not be underestimated for all those patients in which three-drug regimens are not indicated (because they are frail or very elderly, or with significant adverse effects related to proteasome inhibitors).

P15- A CASE OF MULTIPLE MYELOMA PRESENTING WITH CENTRAL NERVOUS SYSTEM PLASMACYTOMA

Denis Bozer[1],Damla Çağla Patır[1],Ajda Güneş[1],Derya Demir[2],Güray Saydam[1],Nur Soyer[1],Mahmut Töbü[1],Filiz Vural[1],Fahri Şahin[1]

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

Objective : Multiple Myeloma (MM) is a disease that takes place as a result of uncontrolled proliferation of clonal plasma cells in the bone marrow. It is possible to see extramedullary plasma cell infiltrates during diagnosis. Central nervous system (CNS) plasmatisomas are extremely rare (occuring in less than 1% of patients with MM). We present a case presenting with CNS involvement in this article.

Methods :

Results : A 51-year-old woman, applies by reasons of severe headache and diplopia. In the conducted cranial MRI; a hypovascular mass lesion measuring 28x36 mm is observed in the anterior of the sphenoid sinus and posterior to the cavernous sinus laterally, filling the pituitary gland. The pathological examination of the taken brain tissue biopys material is evaluated as extraosseous plasmacytoma. The examinations of the patient that is referred to us are evaluated as: Hemoglobin (hb) 12,7 g/dL, creatinine 0,81 mg/dL, albumin 41 g/L, globulin 27 g/L, calsium 10,3 mg/dL, fk/fl 11200 mg/L, free lambda 33 mg/L, free kappa/free lambda 339,3, ig G 9,81, lg A>0,5, lg M 0,38. Based on the pathological examination of the bone marrow biopsy material, the patient was diagnosed with CD38(+), kappa myeloma. In the conducted PET-CT examination, a hypermetabolic soft tissue lesion is observed starting from the anterior clivus and continuing along the posterior wall of the nasopharynx. Additionally, hypermetabolic soft tissue densities filling the ethmoid sinuses and showing continuity to bilateral maxillary sinuses are observed; some of these are subcentimeter-sized multiple hypermetabolic lymph node involvements seen in bilateral cervical chains, as well as axilalry, mediastinal, and abdominopelvic locations. The patient underwent radical radiotherapy of the tumor bed of 40 Gy divided into 20 fractions and boosted up to 50 Gy for residual tumor. The patient is started on bortezomib-pomalidomide-dexamethasone (VPd) treatment. 1% plasma cells are observed in the bone marrow biopsy after 4 cures of VPd. In the response-evaluation purposeful PET-CT examination, the hypermetabolic foci from the previous examination are observed to have fully regressed. Autologous stem cell transplantation is performed in the patient with a full response. At the 1-month post-transplant follow-up visit, the control tests are revealed the following values: free kappa 29.4 mg/dL, free lambda 32.8 mg/L, fk/fl 0.89, lgG 13.6, lgA 0.8, lgM 0.75. These results have been evaluated, and the patient continues to be motinored at our outpatient clinic.

Conclusion: The use of agents that can cross blood-brain barrier (BBB) is important in its treatment of Central nervous system plasmacytomas.Combining radiotherapy with systemic treatment is recommended. Proteasome inhibitors (Pls) (bortezomib, carfilzomib, and ixazomib) cannot cross BBB.its has been reported that when bortezomib is used in combination with other agents, it enhances radiosensitivity and chemosensitivity.its has been reported that when bortezomib is used in combination with other agents, it enhances radiosensitivity and chemosensitivity BBB. Treatment should include agents that can cross the blood-brain barrier (BBB) and may be a valid option for survival extension when combined with a preparative regimen targeting CNS involvement, alongside a second autologous stem cell transplant.).

P16- OCULAR ADVERSE EVENTS AND FUNCTIONAL IMPACT IN TRANSPLANT INELIGIBLE PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA TREATED WITH BELANTAMAB MAFODOTIN IN COMBINATION WITH LENALIDOMIDE AND DEXAMETHASONE (BelaRd Trial)

Ioannis Ntanasis-Stathopoulos[1],Maria Gavriatopoulou[1],Panagiotis Malandrakis[1],Despina Fotiou[1],Magdalini Migkou[1],Foteini Theodorakakou[1],Vasiliki Spiliopoulou[1],Rodanthi Syrigou[1],Evangelos Eleutherakis-Papaiakovou[1],Stavros Gkolfinopoulos[2],Kyriaki Manousou[2],Efstathios Kastritis[1],Meletios A. Dimopoulos[1],Evangelos Terpos[1]

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

Objective : Ocular adverse events (OAEs), manifesting as visual acuity changes, ocular symptoms, and corneal findings, are common with belantamab mafodotin (belamaf; GSK2857916) and the main reason for dose modifications. Here, we present the OAEs and the associated functional impairment in transplant-ineligible (TI), newly diagnosed multiple myeloma (NDMM) patients (pts) treated with an extended dose schedule of belamaf in the phase 1/2 BelaRd study.

Methods : BelaRd (NCT04808037) is an open-label, phase 1/2 study conducted in Greece, aiming to enroll 66 TI NDMM pts. In Part 1, which investigates the safety/clinical activity of belamaf plus Rd, 36 pts are randomized (1:1:1) to receive belamaf at doses of 2.5, 1.9 or 1.4 mg/kg. In this part, belamaf is initially administered q8w and, depending on toxicity, dosing may be rescheduled to q12w. Ocular exams include Snellen best corrected visual acuity (BCVA) and slit lamp corneal evaluation. Ocular symptoms are classified by CTCAE v5.0, while the Ocular Surface Disease Index (OSDI) captures dry eye disease and activities of daily living (ADL). This descriptive analysis included all Part 1 pts (cut-off date 15/04/23).

Results : Among 201/227/192 BCVA assessments in cohorts 2.5/1.9/1.4, a worse than 20/50 result (in the better seeing eye) was observed in 21 (10%)/23 (10%)/18 (9%), while BCVA ≤ 20/200 was noted in 2 (1%)/3 (1%)/11 (6%), with a median time to resolution of 1 month. Across all cohorts, the most frequently reported ocular symptom ≥Gr 2 was dry eye (174/618, 28%), while ≥Gr3 keratopathy was noted in < 2% of assessments. Regarding OSDI, from 186/217/181 responses received, the number of "all/most' of the time worst responses in the ocular symptoms category were 5 (3%)/6 (3%)/8 (4%), while the respective proportions in the ADL category were 6 (3%)/4 (2%)/3 (2%). In terms of missed doses, among 122/129/112 planned belamaf infusions across cohorts, the number of skipped doses due to OAEs were 48 (39%)/41 (32%)/30 (27%). The overall response rate was 100%, no disease progression was observed over a median follow-up of 18.7 months, and 29 (81%) patients achieved at least VGPR while 15 (42%) achieved at least CR, with a median time to first response of 1 month.

Conclusion: Belamaf-Rd, with the extended schedule for belamaf, had a minimal impact in vision-related functioning, as the 'all/most' of the time worst answers in the ADL category of OSDI was < 3% across cohorts. Furthermore, the frequency of clinically relevant impairment in vision was low, as a meaningful BCVA decline was observed in ≤10% of assessments, with a rapid time to resolution. Finally, the treatment combination induced rapid, deep and durable responses across all dose levels. In conclusion, this novel extended belamaf schedule nearly eradicates the risk for clinically relevant ocular toxicity and impact on ADL, without any compromise in clinical activity.

P17- HIGH SERUM BCMA LEVELS EVALUATED BY ELECSYS SBCMA ASSAY AT DIAGNOSIS ARE ASSOCIATED WITH ADVERSE PROGNOSIS IN PATIENTS WITH MULTIPLE MYELOMA

Ioannis Ntanasis-Stathopoulos[1],Panagiotis Malandrakis[1],Aliya Sarmanova[2],Despina Fotiou[1],Katharina Buck[3],Magdalini Migkou[1],Galina Babitzki[3],Evangelos Eleutherakis-Papaiakovou[1],Maria Roussou[1],Maria Gavriatopoulou[1],Meletios A Dimopoulos[1],Efstathios Kastritis[1],Evangelos Terpos[1]

[1]Department of Clinical Therapeutics, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece, [2]Roche Diagnostics International Ltd, Forrenststrasse, 6343 Rotkreuz, Switzerland, [3]Roche Diagnostics, Nonnenwald 2, 82377 Penzberg, Germany

Objective : Serum BCMA (sBCMA) levels have emerged as potential biomarkers for disease monitoring with prognostic value in patients with multiple myeloma (MM).

Methods : We evaluated sBCMA distribution with Elecsys® sBCMA assay (Roche Diagnostics International Ltd, Rotkreuz, Switzerland) and its potential prognostic role in patients with MM and smoldering MM (sMM) by a single institution. Elecsys sBCMA is a quantitative serologic, two-incubation-step assay using the sandwich test format (total assay time of 18 minutes) for the detection of sBCMA in human serum. Patients with sBCMA values outside of measuring range (1.2-900 ng/mL) were excluded.

Results : 166 patients diagnosed from 2018 to 2020 were included (median follow up: 38 months). The median age was 67 years (range 50-93 years), 101 (61%) were males, 122 had symptomatic MM and 44 had SMM. 37 patients (30%) were ISS 1, 44 patients (36%) were ISS 2 and 41 patients (34%) were ISS 3. The baseline mean sBCMA value was 162 ng/mL (SD 169) for patients with MM and 19.4 ng/mL (SD 16.5) for SMM. In a subset of patients with MM, there were available data at the time of first (n=68) and second (n=20) disease progression. At first disease progression, the mean sBCMA value was 102 ng/mL (SD 148), whereas at second disease progression the mean sBCMA value was 169 ng/mL (SD 275). There was a general trend towards decreasing sBCMA values from baseline to first disease progression (mean difference -82.9ng/mL, 95%CI: -118 to -47.8ng/mL, p<0.0001). The sample size was rather small for the second disease progression timepoint (the estimated mean difference of 56.1% which corresponds to a 43.9% decrease from baseline, p = 0.028). The baseline mean sBCMA value was lower in patients without documented disease progression (103 ng/mL, SD 107) compared with patients who had one (200 ng/mL, SD 194) or two (198 ng/mL, SD 185) disease progressions during the follow-up period. In addition, there was no meaningful association between sBCMA baseline values and best response during first line treatment. Furthermore, patients with symptomatic MM were categorized as low (n=61) or high expressors (n=61) based on sBCMA expression at baseline; low expressors had baseline sBCMA values below 113 ng/mL (median) and high expressors had baseline sBCMA values ≥ 113 ng/mL. The median progression-free survival (PFS) was 24.7 months (95%CI: 20.1 to 32.4) for high expressors and 53.7 months (95%CI: 26.9 to not reached) for low expressors (HR 1.67, log-rank p=0.031). In the subgroup analysis according to ISS, a significant association became evident only for patients with ISS 3 (HR 2.24, 95%CI: 1.12 to 4.48, p=0.023, high versus low expressors). Interestingly, high expressors had a median OS of 58.4 months (95%CI: 46 to not reached) compared with low expressors (median OS not reached, HR 2.05, log-rank p = 0.039).

Conclusion: MM patients with high baseline sBCMA levels seem to have a dismal prognosis compared to those with low sBCMA levels. Sequential evaluation of sBCMA in prospective studies will determine the value of incorporating sBCMA measurement in the clinical practice.

P18- EVALUATION OF THE PROGNOSTIC IMPACT OF SECOND LINE ANTI-MYELOMA TREATMENTS ON POST-PROGRESSION OUTCOMES IN THE REAL WORLD-SETTING: THE GREEK MYELOMA STUDY GROUP EXPERIENCE

Eirini Katodritou[1],Dimitra Dalampira[1],Efstathios Kastritis[2],Fotini Theodorakakou[2],Sosana Delimpasi[3],Emmanouil Spanoudakis[4],Ioannis Ntanasis-Stathopoulos[2],Theodosia Papadopoulou[1],Aggeliki Sevastoudi[1],Theodora Triantafyllou[1],Aikaterini Daiou[1],Vasiliki Palaska[1],Kyriaki Tsirou[1],Vasiliki Labropoulou[5],Anastasia Pouli[6],Maria Roussou[2],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 and Bone Marrow Transplantation Unit, Evangelismos Hospital, Athens, Greece, [4]Department of Hematology, University Hospital of Alexandroupolis, Alexandroupolis, Greece, [5]Department of Internal Medicine, Division of Hematology, University of Patras Medical School, Patras, Greece, [6]Department of Hematology, Agios Savvas Cancer Hospital, Athens

Objective : Treatment landscape of relapsed/refractory Multiple Myeloma (RRMM) has improved with the incorporation of monoclonal antibodies, novel proteasome inhibitors and pomalidomide. However, there is limited real-world data regarding the prognostic impact of therapies applied in 2nd line on post-progression survival. Our aim was to describe the treatment approaches in 2nd line and to evaluate post-progression survival parameters i.e., progression free survival (PFS), PFS2 and overall survival (OS) according to different therapies.

Methods : We evaluated 725 RRMM patients (M/F: 349/376, median age: 66, range:38-88) out of 1519 newly diagnosed MM patients with complete staging per International Staging System (ISS) and revised ISS (R-ISS) and complete 1st and 2nd line data, diagnosed between 2003-2022, in Greek Myeloma Centers. A cox regression analysis was used to determine prognostic factors for post-progression OS; post-progression PFS and OS were plotted with Kaplan-Meier; $p<0.05$ was considered as statistically significant.

Results : ISS stage was 1, 2 and 3 in 192, 345 and 188 patients, respectively; R-ISS stage was 1,2 and 3 in 161, 472 and 92 patients, respectively. Data of second revision of ISS (R2-ISS) was available in 75%; R2-ISS stage was 1,2,3 and 4 in 96, 168, 235 and 42 patients, respectively. Induction therapy included conventional chemotherapy or thalidomide-based regimens (CT/TBR; n=211), bortezomib-based triplets (BBR; n=321), lenalidomide-dexamethasone (Ld; n=90), lenalidomide-based triplets (LBT; n=85), daratumumab-based regimens (DBR; n=18); 190/725 patients underwent upfront autologous transplantation (ASCT). Second line therapies were distributed as follows: CT/TBR: 106, BBR: 173, Ld: 204, LBT: 87, DBR: 115, pomalidomide-based regimens (PBR): 40; Patients treated with DBR or PBR were more often Lenalidomide exposed/refractory compared to others (55% and 62% vs. 17% for all others; $p<0.001$). After a median follow up of 63 months (95% CI: 56-69) median post-progression PFS for patients treated with CT/TBR, BBR, Ld, LBT, DBR and PBR in 2nd line was 11, 9, 15, 14, 31 and 16 months, and it was significantly longer for patients treated with DBR ($p<0.05$). Post-progression OS was 20, 23, 33, 40, 42 and 25 months, respectively, and it was significantly longer for patients treated with DBR compared to BBR, CT/TBR, PBR and Ld), however it did not differ compared with patients treated with LBT. PFS2 was 31, 33, 45, 54, 72 and 45 months respectively and it was significantly longer in patients treated DBR compared with others. Univariate cox regression analysis demonstrated that ISS, R-ISS, R2-ISS at diagnosis, ASCT, 2nd line LBT and DBR were significant predictors for post-progression OS; ASCT, R2-ISS and 2nd line treatment with DBR were independent predictors for post-progression OS in the multivariate analysis (HR for ASCT: 0.67, HR for R2-ISS: (I) vs. (IV): 0.33; (II) vs. (IV): 0.31; (III) vs. (IV): 0.50 and HR for DBR: 0.63).

Conclusion: In conclusion, these real-world data demonstrated that treatment with DBR in 2nd line induced a 49% and 37% reduction in the risk for progression or death, respectively, and improved significantly post-progression PFS and OS. First line therapies including LBT did not affect post-progression OS, suggesting that DBR, may mitigate the negative impact of lenalidomide refractoriness.

P19- ISATUXIMAB IN COMBINATION WITH POMALIDOMIDE AND DEXAMETHASONE IN PATIENTS WITH MULTIPLE MYELOMA PROGRESSING ON OR AFTER ONE LINE OF LENALIDOMIDE-CONTAINING THERAPY; A PHASE 2 STUDY

Evangelos Terpos[1],Maria Gavriatopoulou[1],Eirini Katodritou[2],Argiris Symeonidis[3],Anastasia Pouli[4],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],Ioannis Ninos[5],Sosana Delimpasi[6],Eleftheria Hatzimichael[7],Efstathios Kastritis[1],Meletios A. Dimopoulos[1]

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

Objective : Isatuximab combined with pomalidomide and dexamethasone (IsaPomDex) is indicated for the treatment of patients with relapsed/refractory multiple myeloma (RRMM) who have received ≥2 prior therapies including lenalidomide and a proteasome inhibitor. The current study aims to evaluate the efficacy and safety of IsaPomDex in patients with MM relapsing after one line of treatment containing lenalidomide.

Methods : EAE115 (NCT05298683) is an ongoing, investigator-initiated, phase II, prospective, open-label, multicenter study aiming to enroll 108 patients with RRMM at first relapse. Patients receive six 28-day cycles of IsaPomDex at the approved schedule. Following initial 6 cycles, patients achieving at least very good partial response (VGPR) are randomized 1:1 to receive Isa (Q2W or Q4W) plus PomDex, and pts achieving <VGPR continue treatment with Isa (Q2W) plus PomDex. Treatment is given until progressive disease, death, unacceptable adverse events (AEs), lost to follow-up, or consent withdrawal. The study primarily evaluates the overall response rate (ORR) to IsaPomDex therapy at six months. Adverse events are classified using the Medical Dictionary for Regulatory Activities. Herein, we present safety and efficacy data for all treated patients (cut-off date 15/05/23).

Results : Twenty patients had received at least one dose by the cut-off date, of whom 16 (80.0%) were continuing with IsaPomDex treatment; four (20.0%) had discontinued. At baseline, patients had a median age of 72.0 years (range: 60.0–85.0), 10 (50.0%) were male, and 13 (65.0%) had ECOG PS 0. Eleven (55.0%) patients were RISS stage II, 9 (45.0%) patients had lytic bone lesions, 5 (25.0%) had high-risk cytogenetics, and 1 (5.0%) had soft-tissue plasmacytomas. Regarding previous treatment outcomes, 14 (70.0%) patients had achieved ≥VGPR, 2 (10.0%) stringent complete response, 2 (10.0%) complete response; 10 (50%) VGPR. Five (25%) and 1 (5.0%) patients achieved partial and minimal response, respectively. Six (30.0%) patients had received ASCT in the prior line. At a median follow-up of 3.4 (range:0.6–6.1) months, the median number of IsaPomDex cycles received was 3.0 (range:1.0–7.0); one (5.0%) patient received six treatment cycles. Of the 18 (90.0%) response evaluable patients VGPR and PR were achieved by 4/18 (22.2%) and 9/18 (50.0%) patients, respectively. ORR was achieved by 13/18 (72.2%) patients, and the median (range) time from IsaPomDex study dose to first response (≥PR) was 1.0 (range: 0.9–1.3) months. Thirteen (65.0%) patients had ≥1 treatment-emergent adverse events (TEAE). Of these, 10 (50.0%) had a ≥1 grade (gr)≥3 TEAE and 4 (15.0%) had ≥1 gr ≥3 serious TEAE. The most common TEAEs were neutropenia in 9 patients (45.0%), anaemia in 3 patients (15.0%) and fatigue in 3 patients (15.0%). The most common gr ≥3 TEAE was neutropenia in 7 patients (35.0%).

Conclusion: Second-line treatment with IsaPomDex in patients with MM who have progressed on or after one lenalidomide-containing line of treatment appears to be effective, although longer follow-up is needed to assess its efficacy. No new safety signals were observed.

P20- ISATUXIMAB IN COMBINATION WITH BORTEZOMIB, CYCLOPHOSPHAMIDE, AND DEXAMETHASONE, FOLLOWED BY ISATUXIMAB AND LENALIDOMIDE MAINTENANCE IN NEWLY DIAGNOSED PATIENTS WITH MULTIPLE MYELOMA AND SEVERE RENAL IMPAIRMENT; A PHASE 2 STUDY

Evangelos Terpos[1],Efstathios Kastritis[1],Argiris Symeonidis[2],Anastasia Pouli[3],Sosana Delimpasi[4],Eirini Katodritou[5],Eleftheria Hatzimichael[6],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],Kyriaki Manousou[7],Maria Gavriatopoulou[1],Meletios A. Dimopoulos[1]

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

Objective : Anti-CD38 antibodies have been incorporated in the upfront treatment of patients with newly diagnosed multiple myeloma (NDMM). We investigated the efficacy and safety of induction treatment with isatuximab plus bortezomib, cyclophosphamide, and dexamethasone (IsaVCd) in patients with NDMM and severe renal impairment (RI).

Methods : EAE116 (NCT05147493) is an ongoing, prospective, phase II study aiming to enroll ~51 patients. Eligible patients have NDMM and severe RI (estimated glomerular filtration rate [eGFR] <30 ml/min/1.73m2) or in need of dialysis. In induction (six 28-day cycles), patients receive: Isa 10 mg/kg IV (Cycle 1: D1, 8, 15, 22; Cyc 2–6: D1, 15); bortezomib 1.3 mg/m2 SC (Cycle 1: D1, 4, 8, 11; Cyc 2–6: D1, 8, 15, 22); cyclophosphamide 300 mg/m2 IV (Cycle 1: D1, 8, 15; Cyc 2–6: D1, 8, 15, 22); and dexamethasone 40 mg PO or IV (Cycle 1: D1, 2, 3, 4, 9, 10, 11, 12; Cyc 2–6: D1, 8, 15, 22). In maintenance (Cycle 7 onwards), patients receive isatuximab 10 mg/kg IV (D1 of each Cycle) and lenalidomide 10 mg PO (or adjusted according to renal function) daily. The study primarily assesses the renal response rate (RRR, partial renal response or better) at six months of treatment with IsaVCd. Other study objectives assess the overall response rate (ORR; defined as partial response [PR] or better) and the safety of IsaVCd. Herein, we present safety and efficacy data for all treated patients (cut-off date 15/05/23.

Results : Twenty-five patients have been enrolled; 20 (80.0%) are continuing with treatment and five (20.0%) have died. At baseline, patients had a median age of 70.0 years (range 46.0–87.0), 18 (72.0%) were male, and 22 (88.0%) had ECOG PS ≤1. Thirteen (52.0%) patients were at stage II and 12 (48.0%) patients at stage III by the revised International Staging System, 6 (24.0%) patients had lytic bone lesions, 5 (20.0%) patients had high-risk cytogenetics, and 5 (20.0%) patients had soft-tissue plasmacytomas. Seven (28.0%) patients were in need of dialysis. At a median follow-up of 3.9 months (range 0.1–8.3), patients have received a median of 4.0 treatment cycles (range 1.0–9.0). Eight (32.0%) patients have completed ≥ 6 treatment cycles. RRR was achieved by 5/11 (45.5%) patients who had initiated treatment 6 months before the cutoff date. The median time to RR was 2.8 months (range 0.9–7.0). Of the 19 (76.0%) response evaluable patients, 11 (57.9%) achieved ORR (very good partial response: 6 [31.6%]; PR: 5 [26.3%]). The median time to first response was 1.0 months (range 0.9–1.9). Twenty (80.0%) patients had ≥1 treatment-emergent adverse events (TEAE). 10 (50.0%) patients had ≥1 gr ≥3 TEAE and 7 (43.8%) patients had ≥1 gr ≥3 serious TEAE. The most common gr ≥3 TEAE was peripheral neuropathy in 5 patients (20.0%).

Conclusion: Patients with NDMM and severe RI treated with upfront IsaVCd achieve RR consistent with those reported in the literature for patients receiving bortezomib-based therapy, although longer follow-up is needed to assess the regimen's impact on RI. No new safety signals were observed.

P21- PRE-EXPOSURE PROPHYLAXIS FOR COVID-19 WITH TIXAGEVIBAM/CILGAVIMAB (EVUSHELD) IN PATIENTS WITH MULTIPLE MYELOMA IN THE OMICRON SARS-CoV-2 ERA

Ioannis Ntanasis-Stathopoulos[1],Maria Gavriatopoulou[1],Charalampos Filippatos[1],Nikoletta-Aikaterini Kokkali[1],Evangelos Eleutherakis-Papaiakovou[1],Panagiotis Malandrakis[1],Vassiliki Spiliopoulou[1],Rodanthi-Eleni Syrigou[1],Foteini Theodorakakou[1],Despina Fotiou[1],Magdalini Migkou[1],Maria Roussou[1],Efstathios Kastritis[1],Meletios A. Dimopoulos[1],Evangelos Terpos[1]

[1]Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece

Objective : In patients with multiple myeloma (MM), SARS-CoV-2 infection has been associated with severe clinical course and high mortality rates, due to the concomitant disease- and treatment-related immunosuppression. Furthermore, immune response to COVID-19 vaccination is attenuated. Therefore, patients with MM are eligible to receive pre-exposure prophylaxis with tixagevimab/cilgavimab (Evusheld).

Methods : Consecutive patients with MM were prospectively enrolled in the study. All patients had measurement of neutralizing antibodies (NAbs) against SARS-CoV-2 using an FDA approved methodology (enzyme-linked immunosorbent assay, cPass SARS-CoV-2 NAbs Detection Kit; GenScript, Piscataway, NJ, USA) before the administration of tixagevimab/cilgavimab and at one month thereafter. Evusheld was administered at 150mg as two intramuscular injections.

Results : Fifty-five patients with MM were included in this analysis and were followed for a median of 5 months (range 3-6 months) after receiving tixagevimab/cilgavimab. The median age was 63 years (range 36-84), whereas 27 (49%) were females. The majority of the patients had performance status (PS) 0 (n=27, 49%), 22 patients (40%) has PS 1 and 6 patients (11%) had PS 2. Thirty patients (55%) were ISS 1, 17 (30%) were ISS 2 and 8 (15%) were ISS 3. Most patients (n=37, 67%) were at their first line of treatment, 16 (19%) were receiving their second line of treatment, one patient was at the third and one at the fifth line of treatment. Thirty-one patients (56%) had previously received autologous stem cell transplant. At the time of tixagevimab/cilgavimab administration, 19 patients (34%) were receiving combinations including anti-BCMA agents, 24 patients (44%) were receiving combination including anti-CD38 drugs and 12 (22%) were on other treatments. Four patients had a prior history of COVID-19. Regarding vaccination status for COVID-19, 42 patients (76%) had received 4 vaccine doses and 13 patients (24%) had received 3 vaccine shots. All patients were vaccinated with mRNA-based vaccines. The median NAb level before the administration of tixagevimab/cilgavimab was 87% (range 0-98%), whereas it increased to 97% (range 0-98%) at one month thereafter. Overall, 5 patients (9%) were diagnosed with COVID-19 at a median of 1 month (range 1-2) after receiving tixagevimab/cilgavimab. All of these patients received nirmatrelvir/ritonavir (Paxlovid) for 5 days as outpatients along with supportive care as per standard clinical practice and recovered completely. There were no COVID-19-related hospitalization or deaths. Tixagevimab/cilgavimab was well tolerated; no infusion-related reactions or major adverse events were reported. Fifteen patients (27%) experienced pain at the injection site that resolved after a few days.

Conclusion: Tixagevimab/cilgavimab (Evusheld) seems beneficial in patients with MM who had a low incidence of COVID-19 infections during the Omicron wave. No new safety concerns emerged.

P22- REAL WORLD EFFICACY AND TOXICITY OF BELANTAMAB MAFODOTIN: IMPORTANCE OF DOSE INTENSITY AND POST PROGRESSION OUTCOMES

Ioannis Ntanasis-Stathopoulos[1],Panagiotis Malandrakis[1],Irene Solia[1],Foteini Theodorakakou[1],Vassiliki Spiliopoulou[1],Rodanthi-Eleni Syrigou[1],Nikoletta-Aikaterini Kokkali[1],Magdalini Migkou[1],Despina Fotiou[1],Evangelos Eleutherakis-Papaiakovou[1],Maria Roussou[1],Nikolaos Kanellias[1],Maria Gavriatopoulou[1],Evangelos Terpos[1],Meletios A. Dimopoulos[1],Efstathios Kastritis[1]

[1]Department of Clinical Therapeutics, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

Objective : Belantamab mafodotin (belamaf) is a first-in-class B-cell maturation antigen-targeting antibody-drug conjugate (ADC) that has been approved for relapsed/refractory multiple myeloma (RRMM) in patients with ≥4 prior therapies, including proteasome inhibitors (PIs), immunomodulatory drugs (IMiDs) and anti-CD38 monoclonal antibody (MAb). The aim of this study is to provide "real world" data concerning the efficacy and safety of belamaf treatment, as well as, post-belamaf outcomes.

Methods : This is a retrospective study including 36 patients who received belamaf in the Department of Clinical Therapeutics, Athens. The efficacy and safety data were collected prospectively according to our institution's policy. A pre-emptive, but no centralized ophthalmologic examination for ocular toxicity was performed, as in everyday practice.

Results : The median age of the cohort was 68 years (range 41-81) with a median of 5 prior lines (range 3-12). All patients had received ≥two PIs, lenalidomide, pomalidomide and an anti-CD38 MAb and 72% did not respond to carfilzomib, 77% to pomalidomide, 92% to anti-CD38 and 19% to selinexor. Median duration of belamaf therapy was 1.4 months and the starting dose was 3.4 mg/kg and 2.5 mg/kg in 11 and 25 patients, respectively. On intention-to-treat (ITT) overall response rate (ORR) was 36% (13/36; CR:1, VGPR:6, PR:6) with a median progression free survival (PFS) being 3.7 months for the whole cohort and 13 months for the responders (≥PR). The dose reduction of belamaf by at least one level was required in 15 patients who received more than one dose. To adjust for dose delays, relative dose intensity (RDI) was evaluated. Median RDI was 0.7mg/kg/week (range 0.27-1.13) and better PFS was associated with lower RDI; we performed an analysis with patients received at least 3 doses, suggesting that there is a benefit if patients receive lower dose of belamaf with extended dose intervals. A trend for better PFS was also noticed in patients with less than 5 prior treatment lines (8 vs 1.9 months, p=0.126). The median overall survival (OS) after start of belamaf was 15.1 months (14 pts remain alive); 43 months for those with ≥PR and 5 months for non-responding patients. The most common adverse events included keratopathy and ophthalmic toxicity recorded in 47% (Gr2: 17%, Gr3: 19%) of patients and was the main reason leading to dose delays or reductions. Other side effects included infections (19%, Gr3-5 in 11%) and thrombocytopenia (22%, Gr3-4 in 11%). Concerning post-belamaf outcomes, further therapy was given to 24 patients; on ITT, the ORR was 37.5% and the PFS was 3 months.

Conclusion: Our real-world findings are consistent with phase 2 studies concerning the efficacy of belamaf in heavily preteated RRMM patients. Responder patients recorded long remissions and OS and may benefit from dose adjustments. However, patients who relapse on belamaf and receive treatment prior given have moderate results; hence, novel therapies need to be assessed.

P23- MANAGEMENT AND OUTCOMES OF ANTI-CD38 REFRACTORY PATIENTS: THE IMPACT OF RETREATMENT AND OF SUBSEQUENT THERAPIES

Despina Fotiou[1],Foteini Theodorakakou[1],Eirini Solia[1],Ioannis Ntanasis-Stathopoulos[1],Vassiliki Spiliopoulou[1],Panagiotis Malandrakis[1],Rodanthi Syrigou[1],Nikoleta Kokkali[1],Magdalini Migkou[1],Evangelos Eleutherakis-Papaiakovou[1],Maria Roussou[1],Nikolaos Kanellias[1],Maria Gavriatopoulou[1],Evangelos Terpos[1],Meletios A. Dimopoulos[1],Efstathios Kastritis[1]

[1]Department of Clinical Therapeutics, Plasma Cell Dyscrasia Unit, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece

Objective : The management of refractory myeloma (RRMM) patients to anti-CD38-based therapies is challenging despite the increasing treatment options. Moreover, the use of anti-CD38 monoclonal antibodies in earlier lines increases the number of refractory patients to these drugs. Management of such patients is based either in the use of drugs with new mechanisms of action (if available) or in the retreatment with agents or drug classes used in prior lines. We aimed to describe the outcomes of patients with RRMM failing CD38-based therapy.

Methods : A total of 183 consecutive patients with RRMM that received anti-CD38 containing-therapy (index therapy) and relapsed/progressed and received subsequent therapy were included in this study. The patients started treatment with daratumumab or isatuximab-based regimens from 1/1/2015 to 31/12/2021.

Results : The median age of the patients was 68 years (range 35-89); 50% of patients received index anti-CD38 monotherapy (± dexamethasone), while anti-CD38 was given in combination (triplet) with an immunomodulatory drug and proteasome inhibitor (PI) in 25% and 25% of patients, respectively. On index anti-CD38 therapy, overall response rate (ORR) was 55% (CR: 5%, VGPR: 25%, PR: 25%) and median progression free survival (PFS) was 6.4 months: 5.5 months for anti-CD38+/-dexamethasone and 7.4 months for anti-CD38 triplets (p=0.055). After anti-CD38 therapy failure (median 3 prior lines), 40% of patients received PI (23% carfilzomib), 30% pomalidomide, 23% anti-CD38 triplet combinations, 15% belantamab mafodotin, 5% selinexor (+/-PI); 50% received a triplet and 50% a doublet. ORR on the next treatment was 43% with a median PFS of 6.4 months. The corresponding PFS was 4 months for anti-CD38 containing, 6.4 months for PI-based regimens (for carfilzomib 6.7 months), 4.5 months for pomalidomide-based, 6 months for triplets, 6.8 for doublets, while it was 9.1 months for belantamab mafodotin and 3.7 months for the few patients receiving selinexor. The main prognostic factor for PFS post anti-CD38 progression was a PFS ≥12 months during index anti-CD38 treatment and was not associated with the number of prior lines, the type of treatment or pomalidomide resistance. In patients with a PFS ≥12 months during index anti-CD38 therapy, PFS in the line after anti-CD38 failure was 11.6 months. The median overall survival (OS) after anti-CD38 failure was 17.6 months; 12.8 and 22.5 months for patients who failed on antiCD38+/-dexamethasone and anti-CD38 combinations, respectively (p=0.327). The median OS after index therapy was 16.6 months for patients treated with anti-CD38 regimens, 22.9 months for PIs (22.7 months for carfilzomib), 20.9 months for pomalidomide-based treatment, 21 months for triplets, 19.3 months for doublets, 24.5 months for belantamab and 30 months for selinexor. The only significant prognostic factor was PFS≥12 months on index anti-CD38 therapy and the OS after anti-CD38 for these patients was 39 months.

Conclusion: Progression after anti-CD38 therapy is associated with poor outcomes. Novel agents may improve PFS and should be further evaluated especially in triplet combinations. Therapies that have been previously used, including anti-CD38 agents, may be beneficial for selected patients with prolonged remission during initial anti-CD38 therapy; participation in clinical trials should be highly encouraged.

P24- REAL WORLD EFFICACY AND TOXICITY OF SELINEXOR: IMPORTANCE OF DOSE INTENSITY AND POST PROGRESSION OUTCOMES

Panagiotis Malandrakis[1],Eirini Solia[1],Vassiliki Spiliopoulou[1],Ioannis Ntanasis-Stathopoulos[1],Foteini Theodorakakou[1],Rodanthi Syrigou[1],Nicoleta Kokkali[1],Magdalini Migkou[1],Evangelos Eleutherakis-Papaiakovou[1],Despina Fotiou[1],Maria Roussou[1],Nikolaos Kanellias[1],Maria Gavriatopoulou[1],Evangelos Terpos[1],Meletios A. Dimopoulos[1],Efstathios Kastritis[1]

[1]Department of Clinical Therapeutics, Plasma Cell Dyscrasia Unit, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece

Objective : Selinexor is an orally available first in class exportin inhibitor enhancing the therapeutic armamentarium for relapsed or refractory multiple myeloma (RRMM) patients. It has been approved in combination with dexamethasone (Sd) and in combination with bortezomib and dexamethasone (SVd). The aim of this study was to evaluate "real world" data concerning the efficacy and toxicity of selinexor-based treatment and post-selinexor outcomes.

Methods : This is a retrospective study which included 44 RRMM patients treated with Sd (N=21, 48%) or SVd (N=23, 52%) in the Department of Clinical Therapeutics, Athens, Greece. The efficacy and safety of selinexor combinations were evaluated based on the prospective collection of data according to our institute's policy. Toxicity of treatment was managed according to experts guidelines.

Results : The median age of the cohort was 69 years (range 40-89 years) with a median of 6 prior lines of therapy (range 2-14). Starting dose was 40-100 mg per week in 16 (37%) and >100 mg week in 28 (63%) patients. The median duration of selinexor therapy was 2.7 months. On intention-to-treat (ITT), overall response rate (ORR) was 29.5% (13/44, of which CR: 2, VGPR: 3, PR: 8); ORR was 35% for SVd and 24% for Sd patients. In anti-BCMA pretreated patients, ORR was 13% (2/15). Median time to first response was one month (range 0.8-2.9). Median progression free survival (PFS) was 3.0 months for all patients and for the responders (≥PR) was 6.9 months. Median PFS was 2.7 months; 2.7 and 3.4 months for Sd and SVd treated patients, respectively. In starting dose ≤100 mg the PFS was 4 months while in starting doses>100 mg per week the PFS was 2.7 months (p=0.163). Dose reduction of selinexor was required in 56% of patients, but it was not associated with worse PFS. The number of prior lines and prior exposure to anti-BCMA therapy did not affect the PFS. The median overall survival (OS) was 13.7 months. In univariate analysis, serum albumin<3.5 gr/dl (2.1 vs 4.6 months, p=0.001) and LDH>ULN (2.7 vs 3.97, p=0.032) were associated with inferior PFS and OS. However, serum albumin levels were independent with the starting dose of selinexor, dose reduction or prior lines of therapy. After progression to Sd/SVd 20 patients received further therapy; on ITT, the ORR was 40% (8/20) and the subsequent PFS was 3.4 months. The most common adverse event was fatigue (66%), while the most recorded grade 3 or 4 side effect was thrombocytopenia (23%).

Conclusion: Selinexor combinations provide a new treatment option for patients with RRMM, as responding patients have significant probability of longer remission. Serum albumin level seemed a strong prognostic factor according to "real world" data. Moreover, careful, and timely management of the adverse events of the treatment, as well as appropriate dose adjustments may provide additional benefit in this heavily pretreated population.

P25- THERAPY-RELATED MYELOID NEOPLASMS FOLLOWING PARP INHIBITORS: REAL LIFE EXPERIENCE OF A GREEK CANCER CENTER

Evgenia Verrou[1],Prodromos Koutoukoglou[2],Evaggelia Kontana[3],Stavros Gogolopoulos[4],Aggeliki Sevastoudi[1],Aikaterini Daiou[1],Nikolaos Karampatzakis[1],Theodosia Papadopoulou[1],Georgios Douganiotis[3],Dimitra Dalampira[1],Theodora Triantafyllou[1],Efthalia Giannaki[5],Dimitrios Kasarakis[4],Charalambos Andreadis[3],Pavlos Papakotoulas[2],Eirini Katodritou[1]

[1]Hematology Department, Theagenion Cancer Center, [2]1th Oncology Department, Theagenion Cancer Center, [3]3rd Oncology Department, Theagenion Cancer Center, [4]2nd Oncology Department, Theagenion Cancer Center, [5]Hematology Laboratory, Theagenion Cancer Center

Objective : Poly(ADP-ribose) polymerase inhibitors (PARPi) are highly effective as maintenance treatment in Epithelial Ovarian Cancer (EOC). The incidence of therapy-related myeloid neoplasms (t-MN) post PARPi in clinical trials did not exceed 1.2%. However, concerns are rising regarding the development of t-MN following therapy with PARPi in the light of data from a meta-analysis of clinical trials in combination with results from real-world studies. In our knowledge this is the first report of the incidence and the characteristics of t-MN among patients receiving PARPi in the real world setting in Greece.

Methods : We retrospectively analyzed EOC patients who received PARPi as maintenance therapy between 2017-2023 at our institution. Age, type of PARPi, duration of treatment and coexistence of breast cancer were recorded. Regarding t-MN patients immunophenotype analysis, cytogenetics and Next Generation Sequencing (NGS) results, therapy and survival were also reported.

Results : We identified 103 EOC patients treated with PARPi as maintenance with a median age of 58 years (range 28-84). The median number of previous chemotherapy lines and duration of treatment with PARPi were 2 (range 1-9) lines and 12 (range 2-24) months respectively. Breast cancer was a second diagnosis in 14 patients. Olaparib and Niraparib were used in 86 and 17 patients respectively. The incidence of t-MN among patients treated with PARPi was 3.88% (4/103). All patients with a t-MN diagnosis had received Olaparib. A sixty years old patient developed myelodysplastic syndrome with 10% blasts and normal karyotype after 2 lines of previous chemotherapy and 7 months of PARPi exposure. NGS results are pending and she is currently treated with hypomethylating agent. A fifty years old patient was diagnosed with t- MDS/AML with 12% blasts, complex karyotype [42-44,XX,-5,add(7)(q11.2)-17,-17,-18,-20,i(21)(q10),+1-3mar] and normal NGS after 2 previous lines of chemotherapy and 24 months of PARPi exposure. She received 4 cycles of decitabine plus venetoclax achieving complete response. She underwent allogenic stem cell transplantation but died 9 months after the documentation of t-MN. Additionally, 2 patients developed t-AML. A patient aged 69 developed t-AML after 3 lines of previous chemotherapy and 2 months of PARPi treatment and died within 8 days subsequent to the diagnosis of t-AML due to sepsis. A patient aged 48 with a second diagnosis of breast cancer developed t-AML following 3 lines of previous chemotherapy and 24 months of PARPi exposure respectively. Adverse karyotype [45, XX ,(t3;3)(q21;q26), -7] was documented by cytogenetic analysis while NGS revealed mutated SF3B1(VAF ~ 38%). Patient received decitabine plus venetoclax for 8 cycles achieving hematological response and sequentially she was treated with liposomal daunorubicin and cytarabine showing no response. Patient died 11 months subsequent to the diagnosis of t-AML.

Conclusion: In accordance with two previous european real world studies we confirm a high risk of t-MN in EOC patients treated with PARPi associated with unfavorable cytogenetic abnormalities leading to poor prognosis. As PARPi are an emerging therapy for many neoplasms, there is an unmet clinical need to identify patients in increased risk for developing t-MN post PARPi.

P26- EVALUATION OF FERTILITY IN WOMEN TREATED WITH THE R-DA-EPOCH REGIMEN FOR PRIMARY MEDIASTINAL B CELL LYMPHOMA (PMBCL)

A. N. Georgopoulou[1],T.P. Vassilakopoulos[1],P. Panayiotidis[1],N.A. Georgopoulos[2],S. Kalantaridou[3],M. Siakantaris[1],K. Keramaris[1],D. Galopoulos[1],C. Chatzidimitriou[1],A. Kopsautopoulou[1],M. Belia[1],I. Mammali[4],M.K. Angelopoulou[1]

[1]Department of Hematology and BMT of the National and Kapodistrian University of Athens, Laikon General Hospital, [2]Department of Endocrinology of the University Hospital of Patras, [3]B Obstetrics and Gynecology Department of the National and Kapodistrian University of Athens, Attikon General Hospital, [4]2Department of Endocrinology of the University Hospital of Patras

Objective : R-DA-EPOCH and R-CHOP +/- radiotherapy are the most commonly used regimens in PMBCL, a disease that primarily affects young women. The cure rate exceeds 80%. Consequently, treatment-related complications are increasingly recognized, with gonadal failure and amenorrhea playing a fundamental role, causing significant psychological and social impact. This is more prevalent in female patients, in whom collection and cryopreservation of oocytes/ovarian tissue are not applied in everyday clinical practice. Published data are scarce on this subject. The aim of this study is the prospective evaluation of gonadal function in young women with PMBCL who are receiving chemotherapy (CT) with the R-DA-EPOCH regimen. We present our preliminary results on 13 patients.

Methods : Women ≤40 years, receiving first-line treatment with 6 cycles of R-DA-EPOCH, were included. Up to date, 13 patients have been analyzed, with a median age of 27.5 years: 12 PMBCL, 1 grey zone lymphoma. Hormonal measurements were performed at pre-specified time points: before treatment (t0), during CT(t1), at the end of CT(t2) and every six months (t6, t12) thereafter. The following hormones were measured: follicle-stimulating hormone (FSH), lutenizing hormone (LH), progesterone (PG), estradiol (E2), anti-Mullerian hormone (AMH). FSH reflects gonadal function in women (increased levels indicate gonadal dysfunction). AMH is considered to be the most sensitive biomarker for gonadal reserve (decreasing values correlate with ovarian insufficiency). E2 and progesterone are the major sex hormones.

Results : Gonadal damage, reflected by the decrease in AMH, was evident [median values: 16,6pmol/L(t0), 0,16pmol/L(t1), 3,28pmol/L(t2), amh0-1 p=0.005, amh0-2 p=0.028]. AMH values sharply decreased from the beginning to the middle of CT and remained low throughout the treatment period. After the end of CT, AMH remained low, and returned to normal values a year after the end of treatment. In contrast to AMH, no clear alteration was seen with FSH and LH possibly because 50% of the patients received prophylactic treatment with GnRH analogues, that blocks their release from the pituitary. Estradiol and progesterone did not change significantly. As far as the menstrual cycle is concerned, all patients reported cycle disorders, with 80% developing amenorrhea after the first cycle of immunochemotherapy.

Conclusion: Gonadal function in female patients with PMBCL malignant lymphomas is affected by the R-DA-EPOCH regimen. Gonadal dysfunction was evident from treatment initiation and normalized a year after the end of CT, indicating a chemotherapy-dependent genotoxic effect. AMH proved as a more sensitive marker compared to FSH, as it is independent of menstrual cycle phases and of prophylactic GnRH analogue administration.

P27- EVALUATION OF GONADAL FUNCTION IN YOUNG MEN AND WOMEN TREATED WITH ABVD FOR HODGKIN LYMPHOMA (HL)

A. N. Georgopoulou[1],T.P. Vassilakopoulos[1],P. Panayiotidis[1],N.A. Georgopoulos[2],S. Kalantaridou[3],M. Siakantaris[1],K. Keramaris[1],I. Konstantinou[1],M. Arapaki[1],E. Lalou[1],A. Machairas[1],I. Mammali[2],M.K. Angelopoulou[1]

[1]Department of Hematology and BMT of the National and Kapodistrian University of Athens, Laikon General Hospital, [2]Department of Endocrinology of the University Hospital of Patras, [3]B Obstetrics and Gynecology Department of the National and Kapodistrian University of Athens, Attikon General Hospital

Objective : ABVD or esc.BEACOPP +/- radiation are the two main chemotherapy (CT) regimens used as 1st-line treatment for HL patients. As a result of treatment improvement, many long-term survivors and treatment-related complications are being recognized, among which, gonadal insufficiency that plays a fundamental role for future quality of life. Moreover, little is known about the kinetics of gonadal function and sex hormones during CT to safely guide contraceptive measures.

Methods : This is a prospective study of gonadal function in HL patients, with an age limit of ≤40 years in women and ≤45 years in men. We here present the preliminary results on 94 HL patients. Hormonal measurements were performed at pre-specified time points: before treatment (t0), during CT(t1), at the end of CT(t2) and every six months (t6,t12), thereafter.The following hormones were measured: follicle-stimulating hormone (FSH), lutenizing hormone (LH), progesterone (PG), estradiol (E2), anti-Mullerian hormone (AMH) in women and FSH, LH, testosterone, AMH and inhibin–β in men.

Results : The study included 55 men (median age 30 years) and 39 women (median age 29 years) with HL, all receiving first-line treatment with ABVD. In women, FSH showed an increase from the start of CT, peaked in the middle and remained high for up to 6 months after the end: (t0=4,1U/mL, t1=8,8U/mL, t2=7,7IU/mL, t6=6,6U/mL, fsh0-1 p<0,001, fsh0-2 p<0,01, fsh0-6 p=0,05). AMH showed a dramatic decrease in the middle of treatment, its levels remained low until the end: (t0= 2.85ng/mL, t1=0.45ng/mL, t2= 0.62ng/mL, amh0-1 p<0.001, amh0-2 p<0.001), and progressively returned to normal levels 6 months later. Sex hormones were unaffected. In men, FSH increased from the start of treatment, peaked at the end and remained above normal levels 6 months after the end of CT: [t0=3.8IU/mL, t1=11.07IU/mL, t2=15IU/mL, t6=7.4IU/mL; fsh0-1 p<0.001, fsh0-2 p<0.001, t0-6 p=0.001],while it returned to normal levels at 12 months. Surprisingly, both AMH and testosterone increased: AMH increased progressively from the beginning to the end of treatment and remained high up to 12 months after the end of CT:(t0=8,05ng/mL, t1=8.40ng/mL, t2=13.21ng, t6=13,52ng/mL, t12=13,04ng/ml amh0-1 p=0.002, amh0-2 p<0.001, amh0-6 p<0.001, amh0-12 p=0,05). Testosterone increased during treatment and normalized at the end of CT. (t0=407ng/dL, t1=523ng/dL, t2=535ng/dl, t0-1 p=0.001, t0-2 p=0,001).

Conclusion: Gonadal function in HL patients is affected during ABVD in both sexes. In men, spermatogenesis (reflected by increased levels of FSH, is significantly impaired for 1 year after the end of CT, while testosterone transiently increases, possibly as a result of treatment toxicity to Leydig cells. The finding of increasing values of AMH observed in men, in contrast to women, needs further investigation, as its role in the male reproductive system is not sufficiently studied. In women, gonadal dysfunction is evident (rapid decrease in AMH and increase in FSH), but resolves 1 year after the end of treatment. AMH is a more sensitive marker compared to FSH.

P28- THERAPY- RELATED ACUTE MYELOID LEUKEMIA (t-AML) AFTER R-DA-EPOCH FOR PRIMARY MEDIASTINAL B-CELL LYMPHOMA (PMLBCL): A REAL-WORLD MULTINATIONAL STUDY

Vassilakopoulos TP[1],Piperidou A[1],Tsirigotis P[2],Kalpadakis C[3],Poziopoulos C[4],Mellios Z[5],Kaynar L[6],Apostolodis J[7],Zekster M[8],Symeonidis A[9],Giotas A[10],Agathocleous A[11],Liaskas A[1],Akay O[12],Katodritou E[13],Papageorgiou S[2],Tadmor T[14],Mehtap O[15],Gafter-Gvili A[16],Bouzani M[5],Panayiotidis P[1],Ferhanoglu B[17],Angelopoulou M[1],Horowitz N[18],Gurion R[16]

[1]National and Kapodistrian University of Athens, School of Medicine, Laikon General Hospital, Athens, Department of Hematology and Bone Marrow Transplantation, Athens, Greece, [2]Second Propedeutic Department of Internal Medicine, National and Kapodistrian University of Athens, ATTIKON General Hospital, Athens, Greece, [3]Department of Hematology, University Hospital, University of Crete, Crete, Greece, [4]"METROPOLITAN" Hospital, Neon Phaliron, Greece, [5]Department of Hematology and Lymphoma, Evangelismos General Hospital, Athens, Greece, [6]Erciyes University, Kayseri, Turkey, [7]Department of Adult Hematology & Stem Cell Transplantation, Lymphoma Program, King Fahad Specialist Hospital, Dammam, Saudi Arabia, [8]Soroka Medical Center, Beer Sheba, Israel, [9]Hematology Division, Department of Internal Medicine, Patras, Greece, [10]MDH, Msida, Malta, [11]Bank of Cyprus Oncology Center, Nicosia, Cyprus, [12]Department of Hematology, Koc University, Istanbul, Turkey, [13]Department of Hematology, Theagenion Anticancer General Hospital, Thessaloniki, Greece, [14]Department of Hematology, Bnai Zion Medical Center, Haifa, Israel, [15]Kocaeli University, Kocaeli, Turkey, [16]Department of Hematology, Rabin Medical Center, PetachTikva, Israel, [17]American Hospital, Turkei, Turkey, [18]Rambam Medical Center, Haifa, Israel

Objective : While anthracycline-based chemoimmunotherapy -usually the R-CHOP regimen- has been historically the standard of care for PMLBCL, the NCI introduced the intensified R-da-EPOCH regimen, which produced apparently better outcomes in a medium-sized phase 2 trial, while permitting the omission of consolidative radiotherapy. R-DA-EPOCH contains gradually increasing doses of topoisomerase II inhibitors (etoposide and doxorubicin) and the alkylating agent cyclophosphamide, which are potentially leukemogenic. Cases of t-AML after R-DA-EPOCH have been extremely rarely reported. In the original NCI study 1/51 patients (2.0%) developed t-AML, while in the ALLIANCE 50303 trial t-AML-related deaths were recorded in 2/241 (0.8%) patients of an older population (median age 58 years, 45% females). The aim of this study was to evaluate the incidence and potential risk factors of t-AML in PMLBCL patients receiving R-da-EPOCH.

Methods : We performed a retrospective analysis of 292 patients with R-da-EPOCH treated PMLBCL in Hellenic, Israeli, Turkish, Saudi, Cypriot and Maltese centres. The actuarial incidence of t-AML was estimated by the 1-KM method with patients censored at last follow-up, relapse/progression, death without prior relapse/progression or development of another malignant neoplasm, whichever came first. Potential prognostic factors were identified by the log-rank test.

Results : Six cases of t-AML were reported (6/292,2.1%) [Greece 4/146(2.7%), Israel 2/75(2.7%), Turkey 0/34, Saudi Arabia 0/22, Cyprus 0/5, Malta 0/10]. All six patients were females with a median age of 31 years (range; 23-36). The median time from R-da-EPOCH initiation to t-AML was 21.6 months (range;10.4-28.9). Notably, 47% of the 286 leukemia-free patients had follow-up times <28.9 months, which was the latest observed time of t-AML development. Four cases had evidence of MLL rearrangement and two had normal karyotype. R-da-EPOCH protocol was followed strictly in 3/6 t-AML patients and only one reached maximal (6th level) dose level; 4/6 received R-da-EPOCH up to level ≥4 and all 6 reached level ≥3. None received radiotherapy. Three patients remain in prolonged complete remission (CR; >3 years after allo-SCT), two patients are at present under first-line AML treatment and one died despite allo-SCT. In univariate analysis, patients having reached dose level≥4 (7.3% vs 1.7%, p=0.041) and, marginally, females (5.1% vs 0%, p=0.052) experienced higher risk of t-AML. Reaching level ≥3 was also of marginal significance (5.2% vs 0%, p=0.063). Females received -

numerically- less intensive chemotherapy with 28% (versus 35% in males) and 58% (versus 66%) reaching levels ≥4 or ≥3 respectively. On multivariate analysis, reaching level≥4 was nearly significant (hazard ratio 5.37, 95% CI 0.98-29.34, p=0.052).

Conclusion: The risk of t-AML in R-da-EPOCH-treated PMLBCL may have been underrecognized, as the disease is rare and many of the far older individuals enrolled in the ALLIANCE 50303 trial may have not been exposed to leukemogenic chemotherapy doses. Herein we report a worrisome incidence of t-AML (predominantly MLL-related) after R-da-EPOCH for PMLBCL. The occurrence of further events cannot be excluded, because 47% of leukemia-free patients had follow-up times shorter than the latest t-AML occurrence. The risk of t-AML in this young -otherwise cured- population may be more marked in patients reaching level ≥4 and -probably-females.

P29- REAL-LIFE EXPERIENCE WITH RITUXIMAB-DOSE-ADJUSTED EPOCH (R-da-EPOCH) IN PRIMARY MEDIASTINAL LARGE B-CELL LYMPHOMA (PMLBCL): A MULTINATIONAL ANALYSIS OF 290 PATIENTS

Vassilakopoulos TP[1],Piperidou A[1],Horowitz N[2],Mellios Z[3],Kaynar L[4],Zektser M[5],Symeonidis A[6],Giotas A[7],Agathocleous A[8],Kalpadakis C[9],Akay O[10],Atalar S[10],Katodritou E[11],Leonidopoulou T[12],Papageorgiou S[13],Tadmor T[14],Mehtap O[15],Siakantaris M[1],Paydas S[16],Tuglular T[17],Kanellias N[18],Angelopoulou M[1],Karmiris T[3],Gurion R[19],Ferhanoglu B[20]

[1]National and Kapodistrian University of Athens, School of Medicine, Laikon General Hospital, Athens, Department of Hematology and Bone Marrow Transplantation, Athens, Greece, [2]Rambam Medical Center, Haifa, Israel, [3]Department of Hematology and Lymphoma, Athens, Greece, [4]Erciyes University, Kayseri, Turkey, [5]Soroka Medical Center, Beer Sheba, Israel, [6]Hematology Division, Department of Internal Medicine, Patras, Greece, [7]MDH, Msida, Malta, [8]Bank of Cyprus Oncology Center, Nicosia, Cyprus, [9]Department of Hematology, University Hospital, University of Crete, Crete, Greece, [10]Department of Hematology, Koc University, Istanbul, Turkey, [11]Department of Hematology, Theagenion Anticancer General Hospital, Thessaloniki, Greece, [12]Department of Hematology, Sismanoglion General Hospital, Athens, Greece, [13]Second Propedeutic Department of Internal Medicine, National and Kapodistrian University of Athens, ATTIKON General Hospital, Athens, Greece, [14]Department of Hematology, Bnai Zion Medical Center, Haifa, Israel, [15]Kocaeli University, Kocaeli, Turkey, [16]Cukurova University, Balcalı, Turkey, [17]Marmara University, Marmara, Turkey, [18]Department of Therapeutics, National and Kapodistrian University of Athens, Alexandra Hospital, Athens, Greece, [19]Department of Hematology, Rabin Medical Center, PetachTikva, Israel, [20]American Hospital, Turkei, Turkey

Objective : Real-life studies of moderate size have shown satisfactory but less impressive results compared with the original R-da-EPOCH publication for PMLBCL. However, large studies are needed to accurately estimate the real-life efficacy and toxicity of R-da-EPOCH, the use of radiotherapy (RT) and the significance of the compliance with the strict dose escalation strategy of the protocol. The aim of the study was to assess the clinical outcomes after R-da-EPOCH, the use of RT and the impact of protocol compliance in a multinational real-life setting.

Methods : 290 patients up to 65 years old were enrolled from 31 Greek (n=16), Israeli (n=7), Turkish (n=6), Saudi (n=1), Cypriot (n=2) and Maltese (n=1) Centers (patient number 143, 73, 34, 22, 5 and 10 respectively). Consolidative RT was given at the treating physician's discretion and was highly affected by PET/CT results.

Results : The median age of the patients was 33 years (16-63), 63% were females, 38% had B-symptoms, 21% stage III/IV, 17% PS≥2, 83% elevated LDH (34% highly elevated ≥2xnormal). RT was spared in the overwhelming majority of responders. The 5-year Freedom From Progression (FFP) was 85%. However, 6 patients developed therapy-related (t-)AML at 10.5-24 months from treatment initiation, while in 1st remission, and two Hodgkin lymphoma (one as first and one as second relapse). The 5-year overall survival (OS) was 92% with 20 disease-related deaths (1 toxic). Protocol violations were common (56% of 270 patients with available data so far), mainly consisting of insufficient dose escalation despite the absence of prohibitive toxicity. Among 270 patients with available data, 61% reached level ≥3 and 31% ≥4. The 5-year FFP was 88% vs 82% for pts with strict protocol adherence or not (p=0.16); 5-year OS was not also different (91% vs 92%, p=0.74). FFP and OS did not differ according to the final level reached (≥3 or ≥4). A more detailed analysis of outcome according to the degree of protocol violations is currently ongoing. patients with both risk factors according to the prognostic systems including any extranodal involvement and highly elevated LDH (≥2x) or bulk had inferior outcomes but still better than those achieved by R-CHOP in high-risk pts.

Conclusion: In the largest series reported so far for R-da-EPOCH in PMLBCL, FFP appeared somewhat

but not impressively better than the expected with R-CHOP, but this was achieved with the safe omission of RT was in >85% of responders. OS was >90%. The appearance of 6 cases of t-AML among 290 patients is worrisome. Significant dose-escalation violations were recorded in the real-life; their impact on outcomes appears to be modest and is further evaluated.

P30- THE APPLICABILITY OF PROGNOSTIC MODELS UNDER RITUXIMAB-DOSE-ADJUSTED EPOCH (R-DA-EPOCH) IN PRIMARY MEDIASTINAL LARGE B-CELL LYMPHOMA (PMLBCL): A COMPARISON WITH R-CHOP

Vassilakopoulos TP[1],Piperidou A[1],Horowitz N[2],Mellios Z[3],Kaynar L[4],Apostolidis J[5],Symeonidis A[6],Giotas A[7],Agathocleous A[8],Kalpadakis C[9],Akay O[10],Atalar S[10],Katodritou E[11],Leonidopoulou T[12],Papageorgiou S[13],Mehtap O[14],Pangalis GA[1],Paydas S[15],Tuglular T[16],Kanellias N[17],Angelopoulou M[1],Karmiris T[18],Gurion R[19],Panayiotidis P[1],Ferhanoglu B[20]

[1]National and Kapodistrian University of Athens, School of Medicine, Laikon General Hospital, Athens, Department of Hematology and Bone Marrow Transplantation, Athens, Greece, [2]Rambam Medical Center, Haifa, Israel, [3]Department of Hematology and Lymphoma, Athens, Greece, [4]Erciyes University, Kayseri, Turkey, [5]Department of Adult Hematology & Stem Cell Transplantation, Lymphoma Program, King Fahad Specialist Hospital, Dammam, Saudi Arabia, [6]Hematology Division, Department of Internal Medicine, Patras, Greece, [7]MDH, Msida, Malta, [8]Bank of Cyprus Oncology Center, Nicosia, Cyprus, [9]Department of Hematology, University Hospital, University of Crete, Crete, Greece, [10]Department of Hematology, Koc University, Istanbul, Turkey, [11]Department of Hematology, Theagenion Anticancer General Hospital, Thessaloniki, Greece, [12]Department of Hematology, Sismanoglion General Hospital, Athens, Greece, [13]Second Propedeutic Department of Internal Medicine, National and Kapodistrian University of Athens, ATTIKON General Hospital, Athens, Greece, [14]Kocaeli University, Kocaeli, Turkey, [15]Cukurova University, Balcalı, Turkey, [16]Marmara University, Marmara, Turkey, [17]Department of Therapeutics, National and Kapodistrian University of Athens, Alexandra Hospital, Athens, Greece, [18]Department of Hematology and Lymphoma, Evangelismos General Hospital, Athens, Greece, [19]Department of Hematology, Rabin Medical Center, PetachTikva, Israel, [20]American Hospital, Turkei, Turkey

Objective : The rarity of PMLBCL has prevented the development of dedicated, powerful and validated prognostic systems. The International Prognostic Index (IPI) and its age-adjusted variant are of questionable value under R-CHOP±radiotherapy (RT). Recently, we published two potential prognostic systems for PMLBCL1: The first combined the presence of extranodal disease (stage IV or simply extranodal extension; E/IV) with elevated LDH exceeding twice the upper normal limit (LDH>2x) (E/IV-LDH2x model). The second combined E/IV with bulky disease ≥10 cm (E/IV-bulk). The potentially improved outcomes with R-da-EPOCH render the identification of powerful prognostic factors even harder and the applicability of prognostic models questionable. The purpose of the study was to assess the applicability of the E/IV-LDH2x and E/IV-bulk prognostic models in the setting of PMLBCL treated with R-da-EPOCH and minimal use of RT in a multinational real-life setting.

Methods : In Hellenic, Israeli, Turkish, Saudi, Maltese and Cypriot Centers, 290 patients (≤65 years) with PMLBCL were treated under the R-da-EPOCH program. Consolidative RT was given at the treating physician's discretion in a small minority of patients, usually based on PET/CT results. Full data regarding the E/IV-LDH2x and E/IV-bulk models were available in 282 and 271 patients respectively. Survival data were compared numerically with a previously published Hellenic-Cypriot series of 332 PMLBCL patients (≤65 years old) treated with R-CHOP.

Results : The 5-year Freedom From Progression (FFP) after R-da-EPOCH was 84.5%. The 5-year Lymphoma-Specific Survival (LSS) was 91.6%. Protocol violations were common (53%), mainly consisting of insufficient dose escalation despite the absence of prohibitive toxicity. As shown in the table, the distribution of patients with 0,1 or 2 adverse factors in the E/IV-LDH2x and E/IV-bulk models were almost identical in the R-CHOP- and the R-da-EPOCH-treated populations despite the diverse ethnic origin. With less marked differences between the prognostic subgroups and less events, the prognostic models produced statistically significant results of lower magnitude after R-da-EPOCH compared to R-CHOP. Interestingly, patients with no adverse factors by either model had virtually identical 5-year FFP (88-90%) and LSS (95-96% for the E/IV-LDH2x and 98-99% for the E/IV-

bulk model) irrespectively of treatment with R-CHOP or R-da-EPOCH. The use of RT was much more frequent with R-CHOP. Patients with 1 risk factor had 6-11% better FFP in absolute terms and 3-7% better LSS with R-da-EPOCH compared to R-CHOP. Patients with 2 risk factors had 9% better FFP but virtually no difference in LSS (0-5%) when treated with R-da-EPOCH.

Conclusion: Prognostic models derived from R-CHOP-treated populations are also applicable under R-da-EPOCH, although less discriminative. This comparative study suggests that R-CHOP may be sufficient in patients with no adverse factors but the need of RT remains an open question. Patients with one or multiple adverse factors appear to do better than with R-CHOP. The application of the above prognostic models might facilitate the selection of optimal R-da-EPOCH candidates with the hope to avoid severe toxicity, including t-AML.

P31- LITTORAL CELL ANGIOMA; A VERY RARE SPLENIC VASCULAR-STROMAL NEOPLASM DERIVED FROM THE VENOUS SINUSES OF THE SPLENIC RED-PULP PRESENTED AS AN UNUSUAL CAUSE OF MASSIVE SPLENOMEGALY

John V. Asimakopoulos[1],Eliana Konstantinou[1],Gerassimos Tsouroufli[2],Eleftheria Lakiotaki[3],Ioannis Vassilopoulos[1],Dimitrios Galopoulos[1],Marina P. Siakantaris[1],Theodoros P. Vassilakopoulos[1],Penelope Korkolopoulou[3],Panayiotis Panayiotidis[1],Maria K. Angelopoulou[1]

[1]Department of Hematology and BMT Unit,National and Kapodistrian University of Athens, Laikon General Hospital, Athens, Greece, [2]Second Department of Surgery, Propedeutic, National and Kapodistrian University of Athens, Laikon General Hospital, Athens, Greece., [3]First Department of Pathology, National and Kapodistrian University of Athens, Laikon General Hospital, Athens, Greece

Objective : Massive splenomegaly (MS) is defined as the presence of palpable spleen ≥8cm blcm. Although there are several different causes of splenomegaly, MS is caused by specific pathologies; leishmaniasis, chronic myeloid leukemia, myelofibrosis, hairy-cell leukemia (HCL), and primary splenic lymphoma (PSL). Generally, red-pulp disorders, such as cirrhosis/portal hypertension (PH), myelofibrosis and thalassaemias, are characterized by marked pancytopenia even with mild splenomegaly, in contrast to white-pulp ones, such as lymphoma-infiltration and virus infections, in which pancytopenia is evident at later stages of splenomegaly. However, HCL and splenic diffuse red-pulp small B-cell lymphoma may cause marked cytopenia even in the absence of MS.

Methods : Herein, we describe a 62-year-old female patient presented to our outpatient clinic due to microcytic, hypochromic anemia (Hct: 31,2%, Hb: 9,3gr/dl, MCV: 74,5fl, MCH: 22,2pg, MCHC: 29.8gr/dl) that had been worsen despite iron supplementation along with mild thrombocytopenia (platelets: 104K/μL). Clinical examination revealed splenomegaly 26cm blcm, crossing the midline of the abdomen and extending into the pelvis as well as hepatomegaly 4cm below right costal margin. Peripheral blood smear and biochemical control revealed no significant abnormality; lactate dehydrogenase was normal 95U/L (<214). Computed tomography of the chest and the abdomen showed hepatomegaly with 20cm cephalocaudal diameter without focal lesions, and splenomegaly extending to the right abdomen with cephalocaudal and anteroposterior diameter 25.5 and 22cm, respectively with heterogenous contrast enhancement of the spleen parenchyma. PCR for JAK2V617F, CALR and MPL mutations were negative. Bone marrow smear and trephine biopsy were negative for the presence of fibrosis, lymphoma or blast infiltration, and leishmania bodies, while both showed evidence of hypersplenism, such as increased marrow cellularity with trilineage hematopoietic hyperplasia. 18F-FDG-PET demonstrated the absence of pathologically increased focal or diffuse uptake in any body structure. Thereinafter, fibroscan excluded the presence of liver fibrosis, while triplex of the splenoportal axis and magnetic resonance angiography of the abdominal aorta confirmed the diagnosis of PH with normal flow and direction without evidence of thrombosis or collateral pathways.

Results : Three months later, patient's discomfort and pancytopenia were both deteriorated, while PSL could not be sufficiently excluded, though no increased uptake was shown in 18F-FDG-PET. Thus, splenectomy for both diagnostic and therapeutic purposes was decided. Moreover, gastroscopy confirmed the absence of esophageal varices, while liver biopsy did not reveal any specific pathology. Lastly, genetic analysis for thalassemia was negative. Nine months later, laparoscopic splenectomy was performed; spleen surgical specimen was of 21.5x15x9cm dimensions and 2kg weight. Histologic examination revealed the presence of littoral-cell angioma (LCA); an extremely rare morphologic and immunohistochemical distinct entity characterized by anastomosing vascular channels almost completely replacing splenic tissue, diffusely positive for CD31,PGM1 and ERG, while negative for CD8 and CD34.

Conclusion: According to the latest WHO classification of Haematolymphoid Tumours, LCA is a novel "not previously included" entity classified as a spleen-specific vascular-stromal tumor derived from littoral cells of the venous sinuses of the splenic red-pulp. More than one year after splenectomy, the patient is asymptomatic with reactive thrombocytosis in blood counts and without evidence of either inflammation or local and distant relapse.

P32- THE ROLE OF ECP IN CHRONIC GVHD.

Eleni Gavriilaki[1],Eleni Papchianou[1],Ioannis Batsis[1],Alkistis Panteliadou[1],Andriana Lazaridou[1],Despina Mallouri[1],Varnavas Constantinou[1],Giorgos Karavalakis[1],Apostolia Papalexandri[1],Panayotis Kaloyannidis[1],Anna Vardi[1],Christos Smias[1],Achilleas Anagnostopoulos[1],Ioanna Sakellari[1]

[1]George Papanicolaou Hospital Hematology Department - BMT Unit

Objective : Chronic graft-versus-host disease (GVHD) is a severe complication of allogeneic hematopoietic cell transplantation (alloHCT), directly linked to increased morbidity and mortality. Despite novel biologic agents under study or commercial use in this field, corticosteroids and conventional intensified immunosuppressive therapy remain the cornerstone of treatment. Extracorporeal photopheresis (ECP) has been used as an alternative treatment in many centers. We studied the safety and efficacy of ECP in a large real-world cohort of chronic GVHD patients

Methods : We enrolled consecutive patients that received ECP post alloHCT over the last 2 decades (2003-2022) at our JACIE-accredited center. All patients with unrelated or haploidentical donors received thymoglobulin (ATG) 5mg/kg as prophylaxis. GVHD prophylaxis included cyclosporine–methotrexate in myeloablative and cyclosporine–mycophenolate mofetil (MMF) in reduced toxicity/intensity regimens. Before ruxolitinib or ibrutinib availability, MMF, cyclosporine or ATG were commenced as second line treatment in steroid-refractory patients, depending on previous prophylaxis. ECP was mostly administered as third line treatment with 1 session/week for the 1st month, 1 session/2 weeks for 3 months, evaluation of response and 1 session/month for 6 months. Variables included in the analysis were: patient (age, disease) and transplant (donor, graft) characteristics and post-transplant outcomes (infections, GVHD, treatment, overall survival/OS).

Results : We studied 112 patients with moderate or severe chronic GVHD. Only 13 received 4 or less ECP sessions because of severe GVHD-related morbidity and were excluded from further analysis. Median ECP sessions were 17 (6-49). There were no ECP-related adverse events. 67 patients presented with cutaneous sclerosis manifestations, 73 mucocutaneous disease, 36 liver, 42 visceral and 27 lung involvement. ECP was commenced as second line in 35 patients. Ruxolitinib was administered in combination with ECP in 19 patients, while ibrutinib in 2. Bacterial infections were observed in 43 patients, viral in 38 and fungal in 11 patients. Only 19 patients did not show response to ECP. Significantly lower rates of response presented in patients with visceral involvement ($p=0.037$) and earlier post-transplant GVHD diagnosis ($p=0.001$). With a follow-up of 45.2 (5.6-345.1) months, 5-year CI of chronic GVHD-related mortality was 21.2% and was significantly reduced in patients with ECP response ($p<0.001$). 5-year OS was 65.3% and was independently associated with HLA matching ($p=0.011$), higher number of ECP sessions ($p<0.001$), later initiation of ECP post-transplant ($p=0.002$), response to ECP ($p=0.036$) and no relapse ($p=0.001$).

Conclusion: Our data confirm that ECP is safe and effective for chronic GVHD. Even in the era of novel biologics, ECP should be considered early in the course of GVHD, before significant irreversible end organ damage has been established. Combination with other treatments and individualized treatment algorithms remain important unanswered questions in the field of ECP.

P33- CHARACTERIZATION OF THE MOLECULAR SIGNATURE OF HUMAN MONOCYTES IN AGING AND MYELODYSPLASTIC SYNDROME

Maria Grigoriou[1],Christina Maria Rimba[1],Kyriaki Katsiki[1],Nikolaos Paschalidis[2],Athanasios Tasis[1],Ioannis Kotsianidis[1],Ioannis Mitroulis[1]

[1]Democritus University of Thrace, [2]Center of Basic Research, Biomedical Research Foundation of the Academy of Athens

Objective : Aging is associated with maladaptive inflammation and development of diseases like cancer and cardiovascular disease. This study investigates the molecular signature of peripheral blood monocytes in the context of aging and myelodysplastic syndrome (MDS), an age-related disease.

Methods : Peripheral blood mononuclear cell (PBMCs) were collected, from young healthy donors (YC, 20-30 years), elderly healthy donors (OC, >70 years), and low-risk MDS patients. CyTOF and flow cytometry, with specific markers for monocytes, were conducted. Monocytes were then isolated from the three groups for RNA sequencing.

Results : Untargeted analysis by CyTOF demonstrated increased proportion of clusters characterized as naïve CD4+ and CD8+ T cells, expressing CCR7, CD45RA, CD27 and IL-7Ra, and CD8+ T cells expressing high levels of CD161 and pDCs in PBMCs from YC compared to OC. Regarding patients with MDS, we observed an increase in the proportion of a monocytic cell cluster identified as classical monocytes (CD14+CD38+). For this reason, we focused on monocytes and performed flow cytometry. We observed that the proportion of classical monocytes was higher in YC, whereas there was an increase in the frequency of CD14++CD16+ intermediate cells in samples from OC, a cell population with inflammatory properties, and an increase in the proportion of non-classical CD14+CD16+ monocytes in patients with MDS. Moreover, the frequency of CD206+CD163+ M2-like monocytes was increased in OC compared to YC and patients with MDS. We then performed RNAseq on isolated monocytes and we detected 1087 differentially expressed genes (DEG) that were significantly upregulated and 790 that were downregulated (FDR<0.05) in monocytes from YC compared to those derived from OC. Pathway analysis demonstrated that the upregulated in YC DEGs were enriched in RNA polymerase and ribosome biogenesis pathways, whereas the DEGs that were upregulated in OC were enriched in pathways associated with phagocytosis and pathogen clearance, complement and coagulation cascades, IL-17 signaling pathway, NF-kappa B pathway and TNF signaling pathway. Regarding monocytes from OC and patients with MDS, we detected 134 DEG upregulated in OC and 82 in patients with MDS. Pathway analysis showed the upregulated DEGs in monocytes from MDS patients were enriched for pathways associated with antigen presentation and phagosome formation whereas the enriched pathways for downregulated DEGs in monocytes from MDS patients included TNF and IL-17 signaling. DEGs that were downregulated in monocytes from MDS patients included the chemokines CXCL1 and CXCL8 the chemokine receptor CXCR1, the inflammatory genes S100A8 and S100A9 and SELL, whereas the upregulated genes that of the antigen processing pathways were CD209 and the class II major histocompatibility complex genes HLA-DOA, HLA-DPA1 and HLA-DPB1.

Conclusion: Monocytes exhibit a distinct transcriptomic profile in aging, associated with an enhanced inflammatory signature. Interestingly, there is a swift of monocytes in MDS towards an antigen presenting cell population, at least at the transcriptomic level, which is in line with the previously reported increased expression of HLA-DR in monocytes from patients with MDS. This could be attributed to the increased burden of antigens in the bone marrow due to pyroptotic and apoptotic death of clonal cells.

P34- CORNEAL CONFOCAL MICROSCOPY: A NON-INVASIVE TECHNIQUE FOR EVALUATION OF SMALL-FIBER NEUROPATHY IN PATIENTS WITH LIGHT-CHAIN (AL) AMYLOIDOSIS.

Spyridon Fradelos[1],Chrysanthi Bountziouka[2],Adamantia Voudouri[1],Foteini Theodorakakou[3],Despina Fotiou[3],Efstathios Kastritis[3],Panagiotis Kokotis[4]

[1]Opthalmological Center "Athens Eye Experts, Athens, Greece, [2]1st Department of Neurology "Aeginition" Hospital, National and Kapodistrian University of Athens, Greece, [3]Department of Clinical Therapeutics, National and Kapodistrian University of Athens, Greece, [4]1st Department of Neurology "Aeginition" Hospital, National and Kapodistrian University of Athens. Greece

Objective : The accurate detection and monitoring of small-fiber neuropathy (SFN) is of clinical importance in patients with light-chain (AL) amyloidosis. Corneal confocal microscopy (CCM) is a rapid and non-invasive tool appropriate for examining corneal nerve fibers in vivo. There is scarce data regarding the potential role of CCM in assessing small-fiber nerves alterations in patients with AL amyloidosis.

Methods : In this single-center, prospective case-control study we collected images of both corneas of 15 consecutive patients with biopsy-proven light-chain (AL) amyloidosis and 15 age-matched control individuals. All patients underwent examination with the Heidelberg Retina Tomography Confocal Corneal Microscope and all images of the central corneal subbasal nerve plexus were analyzed by using the software ACCMetrics. Valuable parameters as the Corneal Nerve Fiber Length (CNFL), the Corneal Nerve Fiber Density (CNFD) and the Corneal Nerve Branch Density (CNBD) were automatically calculated. All these CCM parameters were compared with Intra-Epidermal Nerve Fiber Density (IENFD) rates according to skin biopsy.

Results : Median age of patients in our sample was 59 years (interquartile range IQR: 8). There was a significant reduction of CNFD (p-value: 0,040) in patients with light-chain (AL) amyloidosis compared to healthy controls. Additionally, CNFL and CNBD tended to be decreased in the group of patients with AL amyloidosis but this did not reach statistical significance (p-value: 0,063 and 0,099 respectively). Reduced CNFD tended also to be associated with restricted IENFD according to skin biopsy in patients with AL amyloidosis (p- value: 0,060).

Conclusion: CCM might offer an advantage of defining the extent of nerve damage and also expedite evaluation of therapeutic efficacy in patients with AL amyloidosis. Larger case-control studies are needed to further establish this potential and the recruitment of patients in the study is ongoing.

P35- A PROSPECTIVE STUDY FOR FAMILIAL PREDISPOSITION TO PLASMA CELL DYSCRASIAS

Christine İvy Liacos[1],Adam S. Sperling[2],Rebecca Georgakopoulou[1],Flora Zagouri[1],Maria Gavriatopoulou[1],Evangelos Eleutherakis - Papaiakovou[1],Magdalini Migkou[1],Nikolaos Kanellias[1],Despina Fotiou[1],İoannis Ntanasis Stathopoulos[1],Evangelos Terpos[1],Nikhil C.Munshi[2],Efstathios Kastritis[1],Meletios A. Dimopoulos[1]

[1]Department Of Clinical Therapeutics, National And Kapodistrian University Of Athens, Greece, [2]Dana - Farber Cancer İnstitute, Harvard Medical School, Boston, Ma, Usa

Objective : To identify and describe familial predisposition for plasma cell dyscrasias (PCDs) we initiated a prospective study with active recruitment of a cohort of patients with PCDs and active screening of their relatives combined with tissue banking and subsequent genetic analysis.

Methods : Patients in the Department of Clinical Therapeutics diagnosed with PCDs were offered enrollment in the study. Following informed consent, first and second degree relatives > 18 years were eligible for screening. A family pedigree was created for each index case with special focus on family history of PCDs, B-cell lymphomas, or other hematologic or solid malignancies. As a control, index cases' spouses were also screened. Screening included serum protein electrophoresis with immunofixation. Samples from affected individuals were profiled using whole genome sequencing (WGS) and unaffected individuals were genotyped using Axiom Arrays. Data were analyzed using Axion Array Suite and plink and GATK toolkit with BWA.

Results : Of 1,084 patients screened for participation in the study, 752 had multiple myeloma (MM), 77 had smoldering MM, 81 a MGUS, 93 Waldenström's Macroglobulinemia and 81 had AL amyloidosis. 176 (16.2%) patients refused to participate in the study, while 44 (4.1%) were ineligible for further screening due to the absence of a living first- or second-degree relative. The median number of screened first or second-degree relatives per index patient was 3 (range 1 to 10). The median age of index cases was 65 years, of offspring 37 years, of second-degree relatives was 65 years, and of spouses was 65 years. The incidence of PCDs among second-degree relatives was 4.5%, while it was 0.6% among offspring. As a control group, the incidence of PCDs among spouses was 2.6%. One additional member with a monoclonal gammopathy was detected in 98 families (11.3%) of which 57 families (6.6%) had a history of at least one additional first- or second-degree relative with a PCD or B-cell malignancy and 41 new cases of monoclonal gammopathy (4.7%) were identified through the screening process. Genetic analysis was performed on the most heavily affected 18 families (103 members), with at least three affected members or early onset disease (PCD diagnosed <age 50) and evaluated 838,750 SNPs. 30 samples were from affected members and 73 from unaffected members. We found eight SNPs that are significantly enriched in affected members with a p-value below the suggestive cut-off of <1e-5. The top candidate was in the untranslated region (UTR) of TSPAN33, a marker of activated and malignant B-cells. We did not detect any significant enrichment in germline mutations in previously reported genes associated with familial PCD risk such as KDM1a, KRAS or DIS3. Further validation is ongoing.

Conclusion: Our active prospective screening approach to identify familial predisposition to PCDs revealed that 11.3% of patients had families with at least one additional affected member and some families had a substantially higher incidence of PCDs with earlier onset. Study of these high-risk families could identify genomic markers which in future may help us define familial predisposition to PCDs.

P36- GENETIC JUSTIFICATION OF COVID-19 PATIENT OUTCOMES USING DERGA, A NOVEL DATA ENSEMBLE REFINEMENT GREEDY ALGORITHM

Panagiotis G. Asteris[1],Amir H. Gandomi[2],Danial J. Armaghani[2],Markos Z. Tsoukalas[1],Eleni Gavriilaki[3],Gloria Gerber[4],Gerasimos Konstantakatos[1],Athanasia D. Skentou[1],Leonidas Triantafyllidis[1],Nikolaos Kotsiou[3],Tasoula Touloumenidou[5],Ioanna Sakellari[5],Nizar Faisal Alkayem[6],Abidhan Bardhan[7],Maosen Cao[6],Liborio Cavaleri[8],Antonio Formisano[9],Deniz Guney[10],Mahdi Hasanipanah[11],Manoj Khandelwal[12],Ahmed Salih Mohammed[13],Pijush Samui[7],Jian Zhou[14],Evangelos Terpos[15],Meletios A. Dimopoulos[15]

[1]School of Pedagogical and Technological Education, Athens, Greece, [2]University of Technology Sydney, Sydney, Australia, [3]Aristotle University of Thessaloniki, Thessaloniki, Greece, [4]Johns Hopkins University, Baltimore, USA, [5]G Papanicolaou Hospital, Thessaloniki, Greece, [6]Hohai University, Nanjing, China, [7]National Institute of Technology Patna, Bihar, India, [8]University of Palermo, Palermo, Italy, [9]University of Naples "Federico II", Naples, Italy, [10]San Diego State University, San Diego, USA, [11]Universiti Teknologi Malaysia, Johor Bahru, Malaysia, [12]Federation University Australia, Ballarat, Australia, [13]American University of Iraq, Sulaimani, Kurdistan-Region, Iraq, [14]Central South University, Changsha , China, [15]National Kapodistrian University of Athens, Athens, Greece

Objective : Complement inhibition has demonstrated promising outcomes in the context of COVID-19 disease treatment approach. Objective of this research is to (1) determine crucial genetic variants associated with complement; (2) employ a novel data ensemble refinement procedure to uncover the optimal pattern of variants that can accurately predict disease outcome.

Methods : Genetic data were collected from 204 patients hospitalized for COVID-19 treatment,124 in intensive care units (ICU) and 80 in COVID-19 general ward at three different referral centers (Georgios Papanikolaou, Attikon, and John Hopkins Hospital) between April 2020 and April 2021. The study utilized next-generation sequencing (NGS) to analyze DNA that was extracted from peripheral blood samples. The analysis focused on a panel of complement-related genes, which included complement factor H/CFH, CFH-related, CFI, CFB, CFD, C3, CD55, C5, CD46, and thrombomodulin/THBD, as well as TMA-associated ADAMTS13 (A Disintegrin and Metalloproteinase with Thrombospondin motifs). Genetic variants were evaluated using a recently introduced alpha-index, which allows for the identification of variants most predictive of the primary outcome. The optimal combination of these variants was determined through the use of an artificial intelligence-based algorithm (DERGA), which employs a suite of other classification algorithms including Decision Trees, Extra Trees Classification, Random Forrest, Gradient Boost, and Gaussian Process Classification for the purpose of maximizing predictive accuracy regarding the disease outcome (ICU vs. non-ICU admission) for patients diagnosed with COVID-19.

Results : This study analysed genetic variants in 204 patients, revealing individual variations ranging from 40 to 161 variants per patient, with a total of 977 variants detected across the cohort. By utilizing alpha-index, the 30 most critical variants were identified. Moreover, DERGA algorithm defined the optimal pattern of these key variants, resulting in 97% accuracy for predicting disease outcomes.

Conclusion: This study demonstrates the utility of the recently introduced alpha-index in ranking a substantial number of genetic variants. This approach enables the implementation of well-established classification algorithms from the field of machine learning, which are integrated through a data ensemble refinement procedure. This procedure effectively and efficiently determines the significance and relevance of the genetic variants in predicting the admission of COVID-19 patients to the ICU, resulting in high prediction accuracy (97%).

P37- EDTA-DEPENDENT PSEUDOTHROMBOCYTOPENIA IN A CHILD WITH VIRAL INFECTION: A CASE REPORT.

Kyriaki Papadopoulou-Legbelou[1],Smaragda Efraimidou[2],Anastasia Kalesi[1],Paraskevi Panagopoulou[1],Marina-Kely Economou[3],Anna Kioumi[2]

[1]4th Department of Pediatrics, Aristotle University of Thessaloniki, "Papageorgiou" General Hospital, Thessaloniki, Greece, [2]Department of Hematology, "Papageorgiou"General Hospital, Thessaloniki, Greece, [3]31st Department of Pediatrics, Aristotle University of Thessaloniki, "Hippokration" General Hospital, Thessaloniki, Greece

Objective : Pseudothrombocytopenia (PTCP) is an invitro phenomenon that leads to spuriously low platelet count (PLT) due to clumping. It occurs in blood samples, anticoagulated with ethylenediaminetetraacetic acid (EDTA) or less commonly other anti-coagulants.EDTA-dependent PTCP is immunologically mediated by class IgG, IgM or IgA antiplatelet autoantibodies against platelet surface glycoproteins,that cause platelet clumping in the presence of the anticoagulant. It is a rare phenomenon, most commonly found in adults and only occasionally in children, mostly in association with viral infections or with certain medications. Although pseudothrombocytopenia, is a benign finding with no clinical significance, it needs to be promptly recognised, as it may lead to the performance of unnecessary tests, delay of surgeriesor incorrect/unsuitable treatments.Exclusion of vonWillebrand disease (vWD) type 2B,is a caveat that should also be highlighted

Methods : We report a rare case of PTCP in a child. A 3-yearold female presented to the emergency department, with a 3-day history of febrile gastroenteritis. Clinical examination was unremarkable. Initial full blood count (FBC) showed thrombocytopenia (PLT=13.000/μl) but the other cell lines were within normal limits. Aperipheral blood smear revealed PLT aggregates (PLT>100.000/μl) in two separate samples. Coagulation studies, as well as blood biochemistry were normal. Previous FBCs at the age of 2 and 3 years-old were unremarkable (PLT: 267.000/μl and 323.000/μl, respectively). Despite negative family history of bleeding disorders, absence of bleeding diathesis, normalprevious PLT counts, further tests were ordered to exclude von vWD type 2B, which were normal. As EDTA-dependent PTCP was suspected, further peripheral blood samples were obtained, using alternative anticoagulants [Heparin, Sodium Citrate, EDTA-plain, EDTA with Amikacin (5 mg/ml)].

Results : The PLT count from tubes with citrate, EDTA+amikacin and heparin had platelet counts of 222.000/μl, 255.000/μl and 96.000, respectively with no clumps in the first two. PLTs counts from plain EDTA sample immediately and one hour post collection showed PLT=21.000 and 12.300/μl respectively. A capillary blood smear (via fingerprick) revealed the presence of small PLT aggregates. The diagnosis of EDTA-induced PTCP was suggested and the patient was discharged being clinically well. The phenomenon was sustained in subsequent follow-up examinations: at first follow-up, 3 weeks later, PLT count was 80.000/μl, with continued presence of clumps but 270.000/μl, in sample collected in EDTA + amikacin tube. It completely resolved 4 months later, with a PLT count of264.000/μl, in plain EDTA tube without any clumps.

Conclusion: EDTA-dependent pseudothrombocytopenia is a rare phenomenon, especially in children. It should be considered in patients that present with isolated thrombocytopenia during an acute viral infection, especially if they are previously healthy, have normal physical examination, and previously normal platelet counts. Simple and non-expensive tests can confirm the phenomenon and avoid invasive investigations, delays of life-saving surgical procedures, or unnecessary treatments. A regular follow-up is recommended, until complete resolution. In equivocal cases, exclusion of von Willebrand Disease type 2B is recommended.

P38- EMD IN RELAPSE; A SINGLE CENTER EXPERIENCE IN THE ERA OF NOVEL THERAPIES.

Konstantinos Giannakas[1],Stavroula Douna[1],Rodanthi Fiorentzaki[1],Evangelos Asmanis[1],Dionisios Stoumpos[1],Maria Kotsopoulou[1]

[1]Metaxa Anticancer Hospital of Piraeus

Objective : Extramedullary multiple myeloma disease (EMD) refers to the presence of myeloma-related tumors or lesions outside the bone marrow, in areas such as soft tissues, organs, or other parts of the body. Typically, multiple myeloma primarily involves the bone marrow and bones themselves, causing symptoms like bone pain, fractures, and anemia. However, in extramedullary multiple myeloma, the cancerous plasma cells can also accumulate and form tumors in various extramedullary sites, which can lead to different symptoms depending on the location of these tumors. Here we report 15 patients with EMD relapse during a five year span in our center.

Methods : Between 2017 and 2022 we studied 15 patients (51-87 years old) that presented with EMD in relapse. We recorded their age at the time of diagnosis, time to relapse, EMD localization, cytogenetic risk, and lines of therapy before and after EMD.

Results : All patients presented with osteolytic lesions and 5/15 had bone-associated plasmacytomas at diagnosis. Cytogenetic analysis was available for 11/15 patients, of which two were high risk and nine were standard risk. With the exception of two patients that relapsed after 8 and 13 years respectively, all other patients relapsed between a span of 13-48 months from diagnosis, two of them with minimal bone marrow involvement. At the time of relapse, 8/15 patients had bone-associated plasmacytomas, 5/15 had bone-associated and bone-independent plasmacytomas and 2/15 had bone-independent EMD. Bone-associated sites included the skull, spinal cord, vertebrae, pleurae, ilium, sacrum, femur and clavicles while bone-independent sites included the retroperitoneum, GI tract, spleen, lung, muscles and pleural effusions. 7/15 patients had received ASCT. 6/15 patients had received only one prior line of therapy before experiencing EMD relapse, 2/15 had two prior lines, 3/15 had three prior lines and 4/15 had four or more lines of therapy. Following EMD relapse, all of them received anti-cd38 based regimens (either DVd,DKd,DVMP,DKPd or Isa-VCD) 7/15 patients received CIT (DCEP or VDT PACE with Daratumumab), 2/15 received XPO1 inhibitor and 2/15 received Belantamab mafodotin (either monotherapy or with pomalidomide). 1/15 patients achieved CR, 3/15 VGPR, 1/15 is in SD and 9/15 progressed during treatment and died, while one patient was lost to follow-up. Not all patients received concomitant radiation therapy (7/15).

Conclusion: Extramedullary multiple myeloma is considered a more aggressive form of the disease compared to the more common form that primarily involves the bone marrow. It might be associated with a poorer prognosis and may require different treatment approaches. Treatment options for extramedullary multiple myeloma may include chemotherapy, targeted therapies, radiation therapy, and in some cases, stem cell transplantation. Still, there are no guideline algorithms for EMD treatment. Nevertheless, we believe, based on our results, that implementation of novel therapies is imperative, thus highlighting the importance of prospective studies on EMD treatment.

P39- THE PROGNOSTIC SIGNIFICANCE OF HYPERLEUKOCYTOSIS AT DIAGNOSIS OF ACUTE MYELOID LEUKEMIA

C Lalayanni[1],S Bountoura[1],V Kanava[1],E Paphianou[1],A. Papalexandri[1],M. Papathanasiou[1],A. Marvaki[1],A Syrigou[1],G Papaioannou[1],A Atanasiadou[1],I. Sakellari[1]

[1]G Papanikolaou General Hospital Haematology Department-BMT Unit

Objective : Acute Myeloid Leukemia (AML) with high white blood cell count is a medical emergency with a high mortality rate and it has historically been associated with poor prognosis.

Methods : We retrospectively studied 555 patients with AML to examine the prognostic value of hyperleukocytosis, its correlation with early mortality and with other disease characteristics, clinical and molecular.

Results : WBC >50.000/μL at diagnosis was present in 112 patients (20%), 61 male and 51 female, with a median age 49 (15-73) years, whereas WBC <50.000/μL was present in 443 patients (247 male, 197 female, median age 48 [14-75y]). All patients received intensive chemotherapy. The same percentage of patients in both groups underwent allogeneic transplantation in CR1 (HCT, 19% vs 20.5%, p=0.81). LDH was higher in the group of patients with WBC>50.000/μL with a median level of 868IU (112-5136), compared to 307IU (98-5800) in the group of patients with WBC<50.000/μL (p=0.04). Patients with hyperleukocytosis were in a significantly lower rate diagnosed with secondary AML (AML-MR or tAML), 15% versus 31% (p<0.001). The FLT3-ITD mutation was present in 39% of tested patients with hyperleukocytosis (33 of 84) compared to 17% (46 of 267) in patients without hyperleukocytosis, p<0.0001. In addition, even though less patients were tested for NPM1 mutations, we have observed a considerable correlation with hyperleukocytosis: 30/47 patients (64%) in the group of WBC>50.000/μl versus 35% (64/183 patients) in the group of WBC<50.000/μl, p<0.001. The presence of a favorable/intermediate/unfavorable prognosis karyotype was analyzed: In patients with hyperleukocytosis the percentages were 13%/57%/10% accordingly, whereas in the rest of the patients the rates were 11%/65%/24% accordingly, with a statistically significant difference in the presence of unfavorable karyotype, p=0.0017. No difference in mortality during induction chemotherapy was observed (TRM, 6% vs 4%, p=ns). Regarding the response to therapy, no significant difference was observed in complete remission rates (74.1% vs 69%, p=ns), and in relapse rates. Similarly, no significant difference was seen in survival: the 5-year disease-free survival (DFS) rate was 31% vs 37.5%, p=0.2, and the overall survival (OS) rate was 33.2% vs 32.3%, p=0.77, in patients with WBC>50.000/μl and WBC<50.000/μl, respectively. The same analysis was conducted by setting the limit of WBC at 100.000/μL. 52 patients were examined, presenting a median WBC 150.000/μl (100.000-300.000)/μL. Only the presence of NPM1 mutation proved to be significantly higher in these patients (42%, p=0.02). In addition, TRM was higher in this group (10%, p=0.016).

Conclusion: In conclusion, hyperleukocytosis at diagnosis of AML did not prove to carry prognostic value, probably due to the co-existance of favorable prognostic factors such as NPM1 mutations and primary AML and rarely a poor prognosis karyotype.

P40- CIRCULATING MIR-16 AND MIR-21 LEVELS IN MULTIPLE MYELOMA (MM); PROGNOSTIC SIGNIFICANCE ON SURVIVAL AND RESPONSE TO LENALIDOMIDE TREATMENT.

Annita-Ioanna Gkioka[1],Maria Tsota*[2],Alexandros Gkiokas[1],Christina -Aggeliki Mitropoulou[2],Aikaterini Palaiokrassa[2],Alexandros Alexandropoulos[1],Mavra Papadatou-Gigante[1],Vsiliki Bartzi[1],Aspasia Koudouna[1],Marina-Thomais Tryfou[1],George V Dedousis*[2],Marie-Christine Kyrtsonis*[1]

[1]First Department of Propedeutic Internal Medicine, Laikon General Hospital, National and Kapodistrian University of Athens,, [2]Department of Nutrition and Dietetics, School of Health Science and Education, Harokopio University, Athens, Greece.

Objective : Despite significant advances in therapeutic options in MM, prognosis is still poor for patients with particular characteristics, not categorized in the existing risk stratification models. MicroRNAs are non-coding RNA class molecules that regulate gene expression, predominantly post transcriptionally and have shown significant value in the pathogenesis of MM. The aim of the current study was to investigate the expression levels in serum of MM patients and their possible prognostic significance.

Methods : We analyzed serum miR-16 and miR-21 levels in 48 newly diagnosed patients and in 35 relapsed/refractory MM (RRMM) patients before Lenalidomide/ Dexamethasone (RD) treatment, as well as in 15 healthy individuals (HI). 42% were women and 58% men with median age 69 yrs (range 40-85), 33% were ISS 1, 28% ISS 2 and 39 % ISS 3. Ig type was IgG in 46%, IgA in 33%, Light- Chain in 17% and other in 4%. Clinical characteristics and laboratory tests were collected after patients' informed consent. Median Overall Survival (OS) of patients was 68 months. Frozen sera from MM patients and HI were used for miRNA detection, followed by Real-Time PCR. miRNA expression was compared to exogenous cel-miR-39-3p. Median value of miRNA levels was used for the survival analysis. To explore the value of difference between miRNA expression at diagnosis and at relapse the ratio miR Relapse/ Diagnosis (Rel/Dx) was calculated. All statistical analyses were performed using SPSS software (version 28.0, IBM, USA). A p value < 0.05 was defined as statistically significant.

Results : Serum expression of miR-16 and miR-21 was significantly decreased in MM patients at diagnosis compared to HI (miR-16 median 0.047 Vs 1.89 and miR-21 median 0.051 Vs 1.59, $p < 0.001$). Expression levels of miR-16 and 21 expression before RD initiation treatment were also significantly down-regulated compared to healthy individuals (miR-16 median 0.100 Vs 1.89 and miR-21 median 0.143 Vs 1.59, $p<0.001$). Improved OS was observed in patients with lower miR-16 levels ($p=0.024$). In RRMM patients, serum miR-21 levels correlated with ISS ($r=0.468$, $p=0.018$), response to treatment (≥VgPR) ($r=0.453$, $p=0.034$) and marginally with Hb ($r=0.377$,$p=0.06$). Expression of Serum miR-16 levels above two (>2) in RRMM patients was associated with response to treatment (≥PR) ($r=0.427$, $p=0.05$). Ratio of miR-16 Rel/Dx above 2 (≥2) was significantly associated with Time to Reponse ($p=0.027$), while ratio of miR-21 Rel/Dx above 2 (≥2) was associated with Time To Next Treatment ($p=0.042$). Relapse to RD after 24 months was significantly correlated to both serum miR-16 Rel/Dx ($p=0.001$) and miR-21 Rel/Dx ratio ($p=0.038$).

Conclusion: In summary, miR-16 and miR-21 were significantly down-regulated in serum of MM patients. Serum miR-16 levels showed prognostic significance of overall survival in newly diagnosed MM patients. Both miR-16 and miR-21 correlated with disease characteristics and response to treatment. *Equall contribution

P41- SOLUBLE CD163: A POSSIBLE SURVIVAL PREDICTOR IN MYELOPROLIFERATIVE NEOPLASMS

Alexandros Alexandropoulos[1],Annita Gkioka[1],Alexandros Gkiokas[1],Mavra Papadatou[1],Vasiliki Bartzi[1],Aspasia Koudouna[1],Maria Tryfou[1],Niki Kafasi[1],Marie Christine Kyrtsonis[1]

[1]Laikon General Hospital, National and Kapodistrian University of Athens

Objective : Tumor associated macrophages (TAMs') have been shown to play a role in the pathogenesis and prognosis of myeloproliferative neoplasms. However, leveraging this prognostic value in a routine clinical setting is challenging. Measurement of soluble products of macrophage activity, such as sCD163, can bridge that gap and provide us with an additional tool to assess patients' outcomes.

Methods : 30 patients with a median age of 70, diagnosed with various myeloproliferative neoplasms (PV =3, ET=15, MF=7, ET to MF progression =3 and MDS/MPN=2) had their frozen sera measured quantitatively for soluble CD163 after informed consent, and compared with 20 healthy individuals. Measurements were done by ELISA (Duo-Set R&D Quantiquine) according to the manufacturer's instructions. The median value was used as the cut-off point. Values above the median were considered high. Median survival of the cohort was 55 months (range 3-208). Statistical analysis was performed with the SPSS v.26 software.

Results : The median sCD163 was 26726 pg/ml (11831- 97286) in healthy individuals, 21626 pg/ml (19776-26596) in PV, 24913 pg/ml (16696-28726) in ET, 30135 pg/ml (19646-upper undetectable level) in MF, 29516 pg/ml (28317-38742) in ET to MF progression, and finally 30386 pg/ml (28966-31806) in MDS/MPN. Taking the cohort as a whole, a high value of sCD163 was statistically significant in predicting poor overall survival ($p<0.0001$), with the myelofibrosis patients having the strongest correlation.

Conclusion: Our preliminary findings suggest a survival marker for CD163 in MPN's.. More research is needed to elucidate the mechanisms of action in the bone marrow microenviroment that promote MPN clone survival and expansion.

P42- THE CLINICAL SIGNIFICANCE OF PLATELET MARKERS AND MORPHOLOGY ON VARIOUS DISEASES

Panagiotis Christodoulou[1],Spyridon Alexis[2],Maria Kasti[3],Georgios Dimakopoulos[4],Andreas Gribaviotis[4],Anargyros Symeonidis[5]

[1]Medical School of Patras, haematology department, MD, Phd researcher, [2]Medical School of Patras, haematology department, PhD Researcher, [3]Medical School of Patras, haematology department, MD, [4]University of Ioannina, MSc in statistics, [5]Medical School of Patras, Professor of haematology, MD

Objective : We have conducted a prospective epidemiological study on the potential clinical significance of platelet markers and how the process of megakaryocytopoesis might be associated with either the inflammatory process or the presence of a neoplastic disorder. Our goal was to take full advantage of the results taken by a simple blood test analysis so as to facilitate the diagnosis and prognosis of disease.

Methods : We have analyzed 1110 samples of patients who were being treated in five general hospitals of Western Greece. The samples were chosen randomly with a goal to reach a fair amount in certain disease categories and a control group of 103 healthy subjects. The samples were analyzed in Sysmex XN 2000 automatic haematological analyser. All of the samples were stained (May Grunwald Giemsa stain) so as to observe the morphology of platelet cells.

Results : Both the platelet number and all the three markers are strongly correlated (p=0) between the three age groups (18-45, 46-65, >65). The same result was found in the comparison of patients with normal platelet count, thrombopenia and thrombocytosis (p=0). Both three platelet markers were strongly correlated (p=0) in comparison with microscopic morphology (large platelets). Last but definitely not least, platelet count (p=0,036), MPV (p=0,029), PDW (p=0), PLCR (p= 0,015) are strongly correlated with the presence of disease in comparison with the control group. The same results were found in the analysis of the samples with abnormal values of MPV, PDW and PLCR.

Conclusion: The study of the morphology of platelets seems to confirm our working hypothesis as high percentages of the presence of both elevated platelet markers and large (activated) platelets are found in the disease group compared to the group of healthy patients (in which the existence of morphological findings was particularly low). It seems that the study of the markers, especially in association with the image from the microscope, can hint to the presence of a disease, so further associations with specific diseases must be made.

P43- EVALUATION OF 26S PROTEASOME ACTIVITY IN PATIENTS WITH MYELODYSPLASTIC SYNDROMES

Georgios Kalampounias[1],Theodosia Androutsopoulou[1],Kalliopi Zafeiropoulou[2],Panagiotis Katsoris[1],Argiris Symeonidis[2]

[1]Department of Biology, University of Patras, [2]General University Hospital of Patras, University of Patras

Objective : Proteasome inhibitors are a group of drugs targeting the Ubiquitin-Proteasome System, the main protein degradation pathway utilized by both, normal and cancer cells. Cancer cells rely heavily on this pathway to replace damaged, misfolded or excessive amount of proteins, as a result of rapid biosynthetic rates, metabolic dysregulation, as well as of elevated Reactive Oxygen Species levels, that lead to the accumulation of oxidized peptides. Altough impairment of the proteasome function is an effective treatment for many hematological malignancies, such as multiple myeloma, Waldenstrom's macroglobulinemia and mantle cell lymphoma, there is no clear evidence to support their administration to patients with Myelodysplastic Syndromes (MDS). MDS are a group of clonal hematopoietic stem-cell disorders, characterized by ineffective hematopoiesis and an elevated risk of transformation to acute myeloid leukemia (AML). The ineffectiveness of proteasome inhibitors in patients with MDS is currently being investigated, though it is not clear whether they rapidly develop resistance to the drug, or the proteolytic activity of the proteasome is constitutively lower in these cells, thus limiting the drug's therapeutic effects. The purpose of this study was to assess the Chymotrypsin-like activity of the proteasome - the main type of proteasomal enzymatic proteolytic activity - in patients with MDS and correlate it with the patient's risk of evolution towards AML transformation.

Methods : Patients with MDS, healthy donors, AML patients (as a positive control for high proteasomal activity) and lymphoma patients without bone marrow infiltration were recruited and grouped according to IPSS score into Lower- or Higher-risk groups (Each group contains 10 subjects). The Lower-risk group included patients with IPSS scores of 0-1, and the Higher-risk group included patients with IPSS scores of ≥1.5. Peripheral Blood Mononuclear Cells (PBMCs) and Bone Marrow Mononuclear Cells (BMMCs) were isolated from the peripheral blood and from bone marrow aspirates, respectively. The samples were analyzed using Western Blot Analysis and Immunocytochemistry to assess the expression of the proteasome subunit β5, which is the principal subunit responsible for the Chymotrypsin-like activity of the proteasome. Another portion of each cell sample was lysed, and the extract was incubated with the proteasome fluorogenic substrate-peptide LLVY-AMC to fluorometrically measure the proteasome activity. The study was approved by the University General Hospital of Patras IRB (17955/20-07-2020). All patients signed a written informed consent before their participation in the study.

Results : Concerning chymotrypsin-like activity, the lower-risk group exhibited significantly lower values on the peripheral blood as compared to the higher-risk MDS group, and the same was also observed on the bone marrow aspirates. Notably, the proteolytic activity of lower-risk patients was also lower compared to healthy subjects. In addition, Western blot analysis and immunocytochemical staining revealed higher expression levels of the proteasome β5 subunit in higher-risk patients on both PBMCs and BMMCs. Between healthy subjects and lower-risk patients, no significant changes in the expression of the proteasome β5 subunit were observed.

Conclusion: Overall, the reduced β5 subunit protein may account for the reduced proteasome activity these patients exhibit and therefore the ineffectiveness of proteasome-targeting therapies.