AHOS 2020

WEB-EVENT

ABSTRACTS

P01. TYROSINE-KINASE INHIBITORS AND ACID-SUPPRESSIVE DRUGS: INTERACTIONS AND OUR PERSPECTIVE

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OBJECTIVE: Molecularly targeted, orally administered anticancer drug therapies such as tyrosine-kinase inhibitors have been introduced in hematology field. Tyrosine-kinase inhibitors (TKIs) are weak bases and their solubility depends on pH level of the environment, in this case scenario gastric pH. Suppression of gastric pH leads to impaired absorption and this results therapeutic failure. We examined the common TKIs that we use in hematological disorders and their interactions with acid-suppressive drugs (ASD).
METHODS: We selected 4 proton pump inhibitors (PPI) (lansoprazole, pantoprazole, omeprazole, rabeprazole), and 2 histamine-2 receptor antagonists (H2 RA) (famotidine, ranitidine), and antacids (calcium carbonate/magnesium carbonate). Then we checked their interactions with 5 TKIs (dasatinib, bosutinib, nilotinib, imatinib, ponatinib). Interactions were analyzed by using 4 drug information resources: Lexicomp Interaction Module, Micromedex Drug Interactions, Drugs. com Interaction Checker and Epocrates Interaction Check (Table1, 2). Lastly, we mentioned our clinical policy
Results: All of the chosen TKIs showed interaction with ASD. We examined severity rating results, documentation support levels and content. Not all of the modules obtained the same interactions and also didn't lead the clinician to same direction. The level of "literature support" must be considered by the clinician and the clinical pharmacist. Only Lexicomp and Micromedex has this feature. Drugs. com also gives references about the subject. Dasatinib, bosutinib and nilotinib was the top interacting members. Especially with dasatinib, the instructions say clinicians should avoid prescribing it with PPIs and H2 RAs. Antacids were the only reasonable option due to their limited acid suppressing effect. Bosutinib and nilotinib also get effected by the pH levels and modules suggest considering therapy modification. In Lexicomp, dasatinib and bosutinib's interaction with PPIs showed good reliability ratings. On the other hand the literature about nilotinib and PPI interaction in Micromedex, it is inconsistent so it is graded "fair". Imatinib and lansoprazole interaction is not about pH levels. As a result of this interaction patients may become volnurable to skin reactions.
CONCLUSION: Cancer patients are prescribed multiple drugs routinely during their treatments and they hospitalized oftenly. For treating or preventing ulcers, commonly PPIs and less commonly H2 RAs are prescribed and people get used to using this drugs as a daily routine but this medications are not innocent as we think. Patients with Tyrosine-kinase refracter disease are prescribed another tyrosine-kinase inhibitors and sometimes this condition can be about the lack of absorbtion of the drug which is related to ASD usage. Understanding and preventing this situation is very important. In our clinic, we don't use PPIs or H2 RAs together with dasatinib or nilotinib or bosutinib. If needed, antacids are our first option. For imatinib users, we choose PPIs other than lansoprazole. Ponatinib has a potential to interacting with ASD and we monitor the therapy response then act about it. Understanding which tyrosine-kinase inhibitors need acid enviroment and how to manage the process in optimal ways, are important. With this perspective, we believe longer and successful treatments can be done. In our clinic we prevent unnecessary ASD prescription. Consequently, we achieve therapeutic success with TKIs. Key Words: Tyrosine-kinase inhibitors, Proton pump inhibitors, drug interactions.
OBJECTIVE: Hypomethylating agents (HMA) such as azacytidine and decitabine are the mainstay of treatment for higher risk myelodisplastic syndromes (MDS). Being cytidine analogues, they are incorporated into DNA of highly proliferating cells leading to genome-wide decrease of methylation levels. Although several putative modes of action have been suggested, the precise mechanism

underlying treatment success or failure remains incompletely understood. One possible mechanism of HMA action is through 'viral mimicry' of transcriptionally repressed endogenous retro elements (EREs), which is thought to trigger innate immune pathways. EREs comprise nearly half of the human genome and their transcriptional activity is repressed by diverse mechanisms including DNA methylation. According to the 'viral mimicry' hypothesis, HMA induce unphysiological levels of ERE transcription in transformed cells, which in turn generated nucleic acid species, such as double-stranded RNAs from complementary ERE transcripts, activating innate immune sensors. Although support and a mechanistic basis for this hypothesis is provided from a number of in vitro studies, in vivo evidence from the clinical use of HMA is currently lacking.

METHODS: To explore the possible involvement of EREs in the HMA mode of action, we have compared the transcriptional profiles of CD34+ HSCs isolated from bone marrow samples of healthy donors (n=9) and patients diagnosed with AML (n=9), chronic myelomonocytic leukemia-II (CMML-II, n=9) or high-risk MDS (n=11). For MDS and CMML, samples were obtained before, 15 days (D15) after the initiation of azacytidine and/or after cycle 6.

RESULTS: Our analysis revealed that ERE transcription, measured as a proportion of the total polyA-selected transcriptome, is globally repressed in untreated MDS and CMML, in line with the proposed epigenetic repression that characterizes these conditions. Treatment with azacytidine had measurable effect in overall ERE transcription in HSCs from MDS and CMML patients, which by the 6 th cycle was raised to levels equivalent to those seen in HSCs healthy controls. Comparable results were also obtained following analysis of a publicly available dataset from CD34+ HSCs isolated from MDS and CMML patients prior to and after the 6 th cycle of azacytidine treatment (GSE76203). However, despite noticeable upregulation of overall ERE transcription relative to gene transcription by azacytidine, the therapeutic response was not correlated with or predicted by ERE activity. Indeed, ERE transcriptional activation was frequently observed in azacytidine-treated patients who failed to respond to treatment, whereas it was frequently low in or absent from patients with complete remission.

CONCLUSION: It remained theoretically possible that a therapeutic response to azacytidine depended on the transcriptional activation of a select few ERE loci with innate immune stimulatory properties, which might have been masked by the analysis of global ERE activity. However, few individual ERE loci differed in their activity between patients who responded or not to azacytidine treatment. Moreover, our analysis failed to detect induction of either interferon-inducible genes or interferon-inducible EREs, irrespective of treatment outcome. Together, our results do not support a role for transcriptional activation of EREs or for innate sensing of their nucleic acid products in the therapeutic response of MDS and CMML patients to azacytidine. Investigation of alternative potential mechanisms of azacytidine is therefore warranted.

P2. ANALYSIS OF PREDICTIVE FACTORS FOR DEVELOPMENT OF POST POLYCYTHEMIA VERA AND POST ESSENTIAL THROMBOCYTHEMIA MYELOFIBROSİS: A SINGLE-CENTRE EXPERIENCE

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OBJECTIVE: In some patients with essential thrombocytopenia (ET) or polycythemia vera (PV), myelofibrosis (MF) develops as a natural evolution of the disease, resulting in post-essential thrombocythemia myelofibrosis (PET-MF) or post-polycythemia vera myelofibrosis (PPV-MF). Predictive factors that may cause MF in the course of PV and ET have been investigated in many studies. Here, in our study, the aim was to analyze the parameters that may effect development of myelofibrosis.
Methods: This study was conducted on PV and ET patients who attended Hematology Department of Diskapi Yildirim Beyazit Training and Research Hospital between 2008 and 2019. A total of 231 patients were retrospectively analyzed. Patients who developed MF during the follow-up were recorded. Patients who developed MF were compared with patients who did not develop MF.
Results: A total of 231 MPN patients, 126 ET and 105 PV, were included in the study. MF developed in 15 (6.4%) patients after mean 226 (95% CI: 199.0-253.0) month follow-up period. In overall patient group, JAK-2 mutant allel burden, lymphocyte count, vitamin B12 levels and grade of bone marrow (BM) fibrosis at diagnosis have also statistically significant impact on the development of MF ($p < 0.05$). MF developed in 6 (5.7%) of total 105 PV patients during the mean 263 month follow-up period. As a result of Logistic regression analysis based on MF status in patients with PV; Hb, Hct, NLR and monocyte values were found statistically significant ($p<0.05$). MF developed in 9 (7.1%) of 126 ET patients after mean 161 month follow-up period. As a result of Logistic regression analysis based on MF status in patients with ET, vitamin B12, presence of splenomegaly and BM fibrosis at diagnosis were found statistically significant ($p < 0.05$)
CONCLUSION: The result of the current study demonstrated that, independently from initial BM fibrosis, splenomegaly and elevated vitamin B12 levels can predict the development of PET-MF, whereas elevated NLR and lower monocyte, Hb and Hct can predict the development of PPV-MF. Patients with those initial predictive factors should be monitored more carefully.

P3. A RARE ENTITY: RICHTER TRANSFORMATION PRESENTED WITH SPONTANEOUS TIBIA FRACTURE

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OBJECTIVE: The most common type of leukaemia in adults is chronic lymphocytic leukaemia (CLL). Richter syndrome (RS) is the transformation of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) into an aggressive lymphoid malignancy. The incidence of RS has been reported to vary from 1% to 9% in large series. CLL most commonly transforms into diffuse large B-cell lymphoma (DLBCL) in 90-95% of cases. RS is generally characterized by an aggressive clinical course that presents with fever without infection, weight loss, night sweats, massive splenomegaly and rapidly enlarging lymphnodes. Richter's syndrome most frequently affects lymphnodes (LN) and bone marrow (BM) but extra-nodal localizations such as the gastrointestinal tract, skin, liver, or tonsils may also be involved. Here in, we reported our unique RS case who presented with bone involvement. To our knowledge, bone involvement in RS has not been previously reported in the literature.
Methods:
RESULTS: A 66-year-old female patient was diagnosed with stage 2 CLL, 2 years ago, was followed up for 18 months with out treatment. At 18 months after the diagnosis, spontaneous bone fracture developed in the right tibia. On radiographic examination, bone lesion was also detected in the fracture line (figure 1-2). Patient operated and the lesion was totaly excised by department of orthopedics and traumatology. Biopsy from the bone lesion showed DLBCL. A PET-CT scan revealed multiple LAP with abnormal FDG uptake in the neck and thorax, in addition to the lesion in the tibia. The patient was diagnosed as ritchter sydrome; stage-4 DLBCL and R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, andprednisone) chemotherapy was planned. After 6 cycles of chemotherapy, the lymph nodes and tibial lesion regressed completely. Also, B symptoms was disappeared. The patient achieved complete remission (CR) according to PET-CT imaging.
Conclusion: RS is a heterogeneus condition that is characterised by an aggressive presentation, with low treatment response rates and very poor survival LN and BM are mainly involved but extra-nodal involvement is also observed. Our patient is the first case of RS with bone involvement. In this context, it is important not to ignore the multisystemic approach in hematological diseases.

P4. HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PATIENTS WITH PAROXYSMAL NOCTURNAL HEMOGLOBINURIA WITH OR WITHOUT APLASTIC ANEMIA: MULTICENTER TURKISH EXPERIENCE

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OBJECTIVE: Although inhibition of complement system at different steps is a promising therapy modality in PNH (paroxysmal paroxysmal nocturnal hemoglobinuria) patients, allogeneic hematopoetic stem cell transplantation (HCT) is still the only curative therapy especially for patients with intractable hemolysis or bone marrow failure. The aim of this study is to evaluate the outcomes of allogeneic HCT in PNH patients with or without aplastic anemia (PNH-AA).

METHODS: 35 PNH / PNH-AA patients who were treated with allegeneic (HCT) in ten transplantation centers in Turkey were retrospectively analyzed. 16 (45.7%) and 19 (54.3%) patients were diagnosed as classical PNH and PNH / AA respectively

RESULTS: 2-year overall survival (OS) and GVHD-free, failure-free survival (GFFS) was 81.2% and 78.1%, respectively. 2 year OS in classical PNH and PNH /AA was 81.3% and% 79.9 (p =0,87), respectively and 2 year GFFS in PNH and PNH/AA was 79% and 76% (0,977) without statistical significance. OS and GFFS rates did not differ between transplantations with matched sibling donor (MSD) and matched unrelated donor (MUD), neither

CONCLUSION: Allo HCT with MSD or MUD is a good option in selected patients with classical PNH and PNH / AA. Especially, patients with debilitating and refractory hemolysis and patients with bone marrow failure might form the excellent group for allo - HCT.

P5. IS THE BODY MASS INDEX RELATED TO PROGNOSTIC FACTORS OF MULTIPLE MYELOMA CASES

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OBJECTIVE: Obesity is a well-known risk factor for malignant tumors and increased body mass index (BMI) is associated with the risk of developing malignancy. In our study, the relationship between BMI and demographic and prognostic factors in Multiple Myeloma (MM) cases was examined.
Methods: The data of 181 MM cases followed between 2010-2020 in the Hematology Clinic of Atatürk Training and Research Hospital with K. Maraş Necip Fazıl City Hospital were analyzed retrospectively. Patients with a BMI value> 24.9 (obese and overweight) at the time of diagnosis were defined as Group 1, and patients with a BMI value of n≤24.9 (n: 63) (normal and below) were defined as Group 2. P-value <0.005 was considered as statistically significant by using SPSS version 18.
Results: 118 of the cases were in Group 1 and 63 were in Group 2. The data of 181 patients with a female / male ratio of 78/103 were used. The median age is 64 years old. In comparison of Group 1 and Group 2 according to their BMI value; 72 (75.8%) of 95 cases with ISS I were Group 1 (p = 0.002). Among 96 cases with beta 2 microglobulin value <5.5 mg / dL, 71 (74%) cases were in Group 1 (p = 0.012), and 90 (76.3%) of 128 cases with hemoglobin value >8 g / dL in diagnosis were inside on the group 1 (P = 0.027). 59 (50%) of 118 cases in Group 1, and 40 (63.5%) of 63 cases in Group 2 (p = 0.047) the cases was included among patients who had CD138 positive plasma cells in the bone marrow ≥%60 ratio. There was no significant statistical relationship between being over 65 years old, gender, presence of B symptom, albumin level <3.5 mg / dL, presence of plasmacytoma, pathological fracture, hypercalcemia, light or heavy chain subgroup, and obese or overweight.
CONCLUSION: In our study, while individuals with overweight or obesity had lower levels of kidney function impairment and anemia, the ISS stage was also found earlier; however, the bone marrow plasma cell ratio was higher in individuals with a normal and below of BMI. Although there are publications showing that obesity has an impact in developing from MGUS to MM; we can associate our findings with the catabolic effect caused by the tumor burden at the time of diagnosis. We think that more comprehensive studies examining the effect of malignant cachexia are needed in MM cases.

P6. IN GERIATRIC PATIENTS DOUBLE FILTRATION PLASMAPHERESIS IS EFFECTIVE AND SAFE PLASMAPHERESIS METHOD

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OBJECTIVE: Therapeutic plasmapheresis exchange (TPE) is an extracorporal blood purification technique designed for the removal of pathogenic substances from the plasma of patients including pathogenic autoantibodies, immune complexes, cryoglobulins and cholesterol-containing lipoproteins. Double Filtration Plasmapheresis (DFPP) is a blood purification process to get rid of pathogenic substances from circulation by using 2 specific filters named plasma separator and plasma component separator for specific diseases. Here, we evaluated DFPP performed in our center in patients with age 18-64 years and >65 years retrospectively. In addition, we compared the elderly patients who underwent DFPP and those who underwent TPE with similar features in terms of processing characteristics, patient performance score and blood tests before and after the procedure.
Methods: 324 DFPP procedures applied to 90 patients and 59 TPE procedures applied to 12 patients in therapeutic apheresis center between January 2010-June 2020, were evaluated retrospectively. Patients underwent DPFF were divided into two groups as 18-64 years and >65 years. All of 12 patients applied TPE, were >65 years old.
RESULTS: A total of 102 patients, of whom 56 (55%) were male and 46 (45%) females, were included. Seventy (68.6%), 20 (19.6%) and 12 (11.8%) patients were applied DFPP with age of 18-64, applied DFPP with age of >65 years and applied TPE in geriatric age, respectively. Diagnosis of procedures, number and percentage of patients with relevant diagnosis are presented in Table 1, for each group. Two hundred fifty-nine (79.9%) DFPP procedures performed to 70 patients with age of 18-64 years and 65 (20.1%) DFPP procedures to 20 patients in age of > 65 years. There no was significant difference in terms of number of apheresis sessions per patient, total blood volume (TBV), total plasma volume (TPV), operation time, levels of pre and post procedure hematocrit, hemoglobin, thrombocyte, albumin and protein between two age groups (Table 2). No major adverse event was observed in both age groups. We also compared the performance of different apheresis technique in geriatric patients, including DFPP and TPE. There was no significant difference in terms of number of apheresis sessions per patient, TBV, TPV, operation time, levels of pre and post procedure hematocrit, hemoglobin, thrombocyte, albumin, protein and pre and post-performance score of the patients (Table 3) in both groups. Estimated median overall survival (OS) was similar in geriatric patients who were applied DFPP and TP; 7.9+14.5 months (95% CI 0-36.3) vs 26.0+29.6 months (95% CI 0-84.0), (p=0.6), respectively (Figure 1). No major adverse event was occurred in geriatric patients with both DFPP and TPE. As expected, median OS was better in patients age of 18-64 who underwent DFPP compared with patients age of > 65 years; p=0.01 (Figure 2).
CONCLUSION: We suggested that DFPP technique is feasible and safe in geriatric patients as patients age of 18-64 years. In addition, DFPP technique provided similar outcome and safety profile compared with TPE in geriatric patients. DFPP may be preferred in geriatric patients for specific indications.

P7. ANALYSIS OF DEMOGRAPHIC DATA AND LABORATORY VALUES OF TROMBOTIC MICROANGIOPATHY CASES: A SINGLE-CENTER EXPERIENCE

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OBJECTIVE: Thrombotic microangiopathies are heterogeneous group of diseases characterized by microangiopathic hemolytic anemia, thrombocytopenia and organ damage caused by microvascular thrombotic plugs. The primary causes are mainly thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS) and atypical hemolytic uremic syndrome (aHUS); malignancy, infection, drug use, pregnancy and severe hypertension are secondary causes.
METHODS: The demographic characteristics and laboratory data of 23 patients who were diagnosed with thrombotic microangiopathy, treated and followed up in internal medicine and hematology clinics between January 2015-June 2020 in Bakirkoy Dr. Sadi Konuk Training and Research Hospital were analyzed retrospectively.
RESULTS: 12 of 23 patients included in the study were female and 11 were male. The female/male ratio was found as 1.09. The mean age of the patient group, whose ages ranged from 20 to 74, was 45. 9 patients (39%) had neurological (blurring, dysarthria, fever, gait disturbance, headache), 4 patients (17.3%) had gastrointestinal (bloody diarrhea, abdominal pain), 3 patients had hemorrhagic (hematuria, petechial rash) and 7 patients (30%) had nonspecific (weakness, nausea, vomiting) symptoms on admission. Neurological symptoms were the most common complaints on admission to the emergency department. When the laboratory values of the patients at the time of diagnosis are evaluated; mean hemoglobin value 7.9 g/dl (5-11.9), mean platelet count 24.4 x103/uL (5-90), mean MCV value 89.2 fL (74-107), mean creatinine level 2,05 mg/dl (0.5-6.68), mean LDH level 1195 UI/L (335-2516), mean indirect biluribin value 1.84 mg/dl (0.2-7.26), mean APTT 33.2 sec (23.4-51), mean PT 14.3 sec (10.7-29.1), mean INR 1.2 (0.87-2-31) and mean fibrinogen level was 314 mg/dl. When classified according to blood groups, 9 patients had 0 Rh (+) (40%), 7 patients had A Rh (+) (30%), 6 patients had A Rh (-) (26%) and 1 patient had B Rh (+) (4%) blood group. All patients received 1 mg/kg/day methylprednisolone treatment and therapeutic plasmapheresis was administered. The average number of plasmapheresis sessions was 12 (2-27) and the average number of fresh frozen plasma products used was 20 (13-28). 19 (82%) of 23 patients were diagnosed as thrombotic thrombocytopenic purpura, 2 patients as hemolytic uremic syndrome and 2 patients (9%) as atypical hemolytic uremic syndrome. 19 patients (83%) were discharged on average in 16 days with treatment response and 4 patients (17%) died.
CONCLUSION: We aimed to contribute to the literature with single-center data of our patients diagnosed with thrombotic microangiopathy, which is a disease group with high mortality, since the probability of thrombotic thrombocytopenic purpura cannot be excluded with clinical and laboratory findings on admission. We plan to provide healthier data with the increasing number of patients in the future.

P8. MEAN PLATELET VOLUME AS A PREDICTIVE AND PROGNOSTIC FACTOR FOR PATIENTS WITH ACUTE MYELOID LEUKEMIA: MULTICENTRE RETROSPECTIVE ANALYSIS

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OBJECTIVE: Despite the high number of established risk factors, only few predictive markers exist which can truly aid therapy decisions in patients with AML. The aim of the current study was to examine the impact of easily available common laboratory parameters on the course and prognosis of the patients with AML.
METHODS: Using these data, demographic and clinical characteristics, response assessments and survival rates were analyzed. The impact of the parameters on survival was analyzed.
RESULTS: A total of 148 patients were included in this study. The mean age of the patients was 59±16 years and 81 (% 54.7) were male. The median follow-up period was 7.4 [2-87] months. According to Keplein Meier survival analysis, median overall survival (OS) was 9.2 [5.8-12.6] months, and median progression-free survival (PFS) was 8.6 [6.0-11.2] months. Gender, initial BM blast percentage, mean platelet volume (MPV), lymphocyte-to-monocyte ratio (LMR), treatment regimen and CR1 achievement were found to have a statistically significant effect on both OS and PFS ($p < 0.05$). Patients with CR1 had lower age, good ECOG performance status, lower MPV, lower LDH and received mostly intensive induction treatment than patients without CR1 ($p<0.05$). According to logistic regression analysis, only MPV, LDH and initial treatment status were found to have a significant effect on CR1 achievement ($p < 0.05$).
CONCLUSION: According to the results of the current study, besides the induction regimen, only MPV is demonstrated to effect short and long term outcome including both CR achievement, OS and PFS. Patients with higher MPV at the time of diagnosis should be monitored more carefully.

P9. SCREENING OF ACQUIRED VON WILLEBRAND DISEASE AND FREQUENCY OF BLEEDING IN BCR-ABL NEGATIVE CHRONIC MYELOPROLIFERATIVE DISEASES

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OBJECTIVE: It was aimed to determine the acquired Von Willebrand disease (AVWS) and bleeding frequency in patients with Bcr-abl negative CMPN. It was also aimed to investigate the determining risk factors for bleeding and AVWS development.
METHODS: In this cross-sectional study, a total of 50 patients including 20 ET, 20 PV, 10 PMF, who applied to the adult hematology clinic of Manisa Celal Bayar University Medical Faculty and whose diagnoses were revised according to the last updated WHO 2016 criteria were included. Patients were tested for complete blood count, peripheral smear, blood group, prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen, Factor VIII, VWF antigen level (VWF: Ag), Ristocetin cofactor activity (Rcof) and bleeding time tests. The diagnosis of acquired Von Willebrand disease was made on patients who met three criteria; a) VWF Ristosetin cofactor level is below the reference range according to blood group b) VWF: Rcof/VWF: Ag ratio <0.7 c) Exclusion of hereditary Von Willebrand disease based on no personal and familial bleeding disorder. Patients with and without concomitant AVWS were compared in terms of available treatment options, laboratory parameters, demographic features, blood group, clinical symptoms. Likewise, patients with and without bleeding were compared in terms of available treatment options, laboratory parameters, demographic features, blood group, and clinical symptoms.
RESULTS: AVWS developed in 55% (n=11) of patients in the ET group, 20% (n=4) in the PV group and 20% (n=2) in the PMF group. AVWS was most frequently detected in the ET group among Bcr-abl negative chronic myeloproliferative neoplasms. The mean age of the group with AVWS was significantly lower than that of the group without AVWS. Bleeding was present in 65% of the patients with AVWS and 39.4% of the patients without AVWS. Although bleeding was more common in the group with AVWS, no statistically significant difference was found. Platelet levels of patients with AVWS were found statistically significantly higher than patients without AVWS. The mean platelet count of the group with AVWS was 526.2±233.5 x103/µL, and the mean of the group without AVWS was 354.4±207.8 x103/µL. Bleeding occurred in 35% (n = 7) patients in the ET group, 45% (n=9) in the PV group and 80% (n=8) in the PMF group. Both bleeding and thrombosis development rates were significantly higher in patients with splenomegaly during diagnosis. LDH levels at the time of diagnosis were significantly higher in patients with bleeding.
CONCLUSION: There is no risk classification and threshold platelet count that can be used for AVWS development. In our study, platelet levels of patients with AVWS were found to be statistically significantly higher than patients without AVWS. AVWS testing is recommended for every patient with CMPN and bleeding. In conclusion, large-scale and multicentre studies with more patients are needed to determine the frequency of AVWS and to reveal risk groups in Bcr-abl negative chronic myeloproliferative neoplasms.

P10. RUXOLITINIB INDUCED LEUKOCYTOCLASTIC VASCULITIS: CASE REPORT

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OBJECTIVE: Ruxolitinib is an oral Janus kinase (JAK) inhibitor, which is used in chronic myeloproliferative neoplasms (MPN), especially in primary myelofibrosis (PMF). The beneficial effects of the drug are basically alleviation of B symptoms (as drenching night sweats, weight loss and fever) and decrease of spleen volume. It has also anti-inflammatory and immunosuppressive features. The drug has various adverse effects (AE) such as cytopenia, diarrhea, transaminitis, propensity to opportunistic infections but as far as we know, vasculitis is not one of them. Herein we report a PMF diagnosed patient who developed leukocytoclastic vasculitis under ruxolitinib treatment.
METHODS: Seventy-four year old male patient was diagnosed PMF in April 2019 according to the World Health Organisation 2016 diagnostic criteria (due to presence of megakaryocytic atypia, increase of reticular fiber degree as +3 in the bone marrow, JAK-2 mutation positivity and exclusion of other MPN's). He had a splenomegaly size as 29 cm, detected by ultrasound. His Dynamic International Prognostic Scoring System Plus score was determined as 3 (Intermediate-2). He had previous treatments of thalidomide and prednisolone and subsequently cladribine. Ruxolitinib therapy started in November 2019 with the dose of 10 mg twice daily. He has benefited from ruxolitinib without any AE for 7 months, until multiple nodular erythematous lesions were appeared at both legs. The biopsy showed leukocytoklastic vasculitis. No finding supportive of internal organ involvement was detected. Antinuclear antibody (ANA) in the blood was negative. The lesions regressed rapidly in a couple of days after ceasing ruxolitinib.
RESULTS: Leukocytoclastic vasculitis is an immune complex mediated vasculitis of small vessels' of the skin with rare internal organ involvement and can be mainly infectious or drug related. Prominent causes of drugs are hydralazine, minocycline, propylthiouracil, penicillins, cephalosporins, sulfonamides, phenytoin, and allopurinol. The most dermatologic AE of ruxolitinib is bruise with the 23% frequency. As far as we know no small vessel vasculitis is reported in the literature so far. Due to immunosuppressive and anti-inflammatory effects of the drug, it's unexpected to be a trigger of immune complex condition. In addition, JAK- signal transducer and activator of transcription (STAT) inhibitors as ruxolitinib is being used or under investigation for the treatment of dermatologic inflammatory diseases such as atopic dermatitis, psoriasis or cutaneous graft versus host disease. Regarding our patient, there was no other possible etiology apparent to cause vasculitis and regression of the lesions rapidly with only ceasing the drug and without any anti-inflammatory treatment was considered highly supportive of drug-vasculitis relationship.
CONCLUSION: Ruxolitinib is a novel drug with highly beneficial effects on symptoms, reducing spleen size and decreasing mortality. The data about its AE's are restricted due to relatively lower experience because of its novelty. Although this AE contradicts the mechanism of ruxolitinib, the clinicians should be aware of this easily manageable situation.

P11. A RARE CAUSE OF MONOCLONAL GAMMOPATHY: GAUCHER DISEASE

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OBJECTIVE: Gaucher disease (GH) is an autosomal recessive glycolipid storage disease characterized by the accumulation of glucocerebroside in macrophages, which develops as a result of genetic deficiency in the activity of β-glucocerebrosidase. Among all types of cancer, especially the incidence of multiple myeloma is common in GH and is approximately six times higher than in the general population. MGUS (monoclonal gammopathy of undetermined significance) is an asymptomatic premalignant plasma cell dyscrasia. In the literature, its association with Gaucher disease has been reported in the form of anecdotal cases. In this case, we aimed to present the coexistence of Gaucher disease with MGUS.
METHODS: Case Report
RESULTS: A 45-year-old female patient presented with the complaints of malaise, early satiety, and intermittent abdominal pain. There was no disease or using drug except for hepatomegaly and splenomegaly. The laboratory results were as follows: leukocyte, 5900 /mm3; hemoglobin, 9.2 g/dL; thrombocytes, 67000 /mm3; ferritin, 33 mg/dL; B12 and folic acid levels were in the normal ranges, and albumin, 4.3 mg/dL; globulin: 4.7 mg/dL. The peripheral blood smear showed anisopoikilocytosis, acanthocytes and partly dacrocytes. On the abdominal ultrasonography, the anterior-posterior diameter of the liver was 190 mm. The diameter of the spleen was 240 mm, and multiple undemarcated lesions were visualized in the spleen parenchyma. The Magnetic Resonance Imaging showed multiple nodular structures with a diameter of 6.5 cm in the caudal part of the splenic hilum. In the bone marrow biopsy, clusters of lipid-laden macrophages with large cytoplasm with wrinkled appearance were displayed in most areas, and it was evaluated as a storage disease infiltration. The genetic analysis for Gaucher disease revealed heterozygous n370 s and heterozygous l444 p mutation. The patient was initiated on imiglucerase enzyme replacement with the diagnosis of Gaucher disease. On ERT treatment, the size of the spleen was 140 mm, and leukocyte was 6600/mm3, hemoglobin was 12.6 g/dL, and platelet was 146000/mm3. The 6 th year of follow-up laboratory tests showed that calcium: 11.9 mg/dL, total protein: 9 g/dL, albumin: 4.3 g/dL, globulin: 4.7 g/dL, and proteinuria in 24-hour urine. Monoclonal band was detected in the patient's protein electrophoresis and IGG kappa monoclonal protein was detected in the serum immunofixation electrophoresis. (IgG 2 g/dL, IgA 0.40 g/dL, IgM 0.26 g/dL in serum). The bone marrow biopsy showed 6% clonal plasma cells. On PET-CT, no lytic lesion was visualized. The patient was diagnosed with MGUS. The patient's enzyme replacement therapy and follow-up for MGUS.
CONCLUSION: The relationship between Gaucher disease and plasma cell neoplasms characterized by monoclonal immunoglobulin production has been known for some time. Increased levels of proinflammatory cytokines in GH, the increase in major cytokines responsible for the growth and survival of myeloma cells, especially IL-6, and accordingly clonal B-cell expansion are thought to play a role in the etiopathogenesis. ERT is likely to have a beneficial effect on preventing the emergence and progression of gammopathies. Therefore, adult patients with GH should be carefully followed up for the development of cancers, particularly multiple myeloma.

P12. A CASE OF IBRUTINIB EXPERIENCE IN MANTLE CELL LYMPHOMA

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OBJECTIVE: Bruton's tyrosine kinase (BTK) is a mediator of the B-cell-receptor signaling pathway implicated in the pathogenesis of B-cell cancers. Ibrutinib is a BTK inhibitor, showed antitumor activity in several types of non-Hodgkin's lymphoma, including mantle-cell lymphoma (MCL).
METHODS: We presented a case with relapse and refractory MCL.
RESULTS: We evaluated a case with MCL in July 2015. She was 70 years old at the diagnosis. She had bone marrow involvement. The stage was IVB. The MIPI score of the patient was high. She had hypertension and diabetes mellitus as a comorbidity in background. The patient had received RCHOP therapy in the first line. The time of the relapse was November 2016. We applied rituksimab and bortezomib therapy for relapse disease. The patient didn't come to the clinic till February 2019. We planned RCHOP/RDHAP alternate therapy and autologous stem cell transplantation for second relapse. She didn't tolerate RDHAP therapy. We appealed for off label ibrutinib therapy for refractory disease. The therapy wasn't approved, the patient had received rituksimab and bendamustine therapy. The disease was still refractory. Ibrutinib therapy was approved as off label. After ibrutinib therapy, the disease was remission. She had tolerated ibrutinib. Now, she is receiving 8 th cycle of ibrutinib. We planned to ibrutinib therapy till to progression.
CONCLUSION: Ibrutinib therapy is an effective agent for relapse and refractory disease in MCL. The favorable toxicity profile suggests that ibrutinib provides the opportunity for treatment than current regimens.

P13. ELTROMBOPAG AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: SINGLE CENTER EXPERIENCE

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OBJECTIVE: Poor graft function (PGF) is a life-threatening complication that occurs in 5-27% of the patients following allogeneic hematopoietic stem cell transplantation (allo-HSCT). Eltrombopag is an oral non peptide agonist that binds to a transmembrane site on thrombopoietin receptor.
METHODS: This retrospective analysis included 15 patients receiving eltrombopag for secondary PGF after allo-HSCT during a period from August 2017 to March 2020. Secondary PGF (sPGF) was defined as: presence of persistent thrombocytopenia (<20 × 109/L) at >35 days from HSCT, with or without other cytopenias, with full donor chimerism. Complete response (CR), as defined by platelet ≥ 50 × 109/L, neutrophil ≥1.0 × 109/L, and hemoglobin ≥ 9 g/dL, without blood cell transfusion or granulocyte colony stimulating factor for ≥ 7 consecutive days. Partial response (PR), as defined by hematopoietic engraftment of at least two lineages (platelet ≥ 20 × 109/L, neutrophil≥ 0.5 × 109/L and hemoglobin ≥7 g/dL).
RESULTS: There were 11 male and 4 female patients. Indications for allo-HSCT were acute myelogenous leukemia (AML)/myelodysplastic syndrome (MDS) in 6 patients (40%), acute lymphoblastic leukemia in 4 patients (26.7%), primary myelofibrosis in 2 patients (13.3%), and other diseases in 3 patients (20%). The median patient age was 53 (23- 66) years. Ten patients received myeloablative, and 5 patients received reduced-intensity conditioning. The median duration was 92 (41-276) days from transplantation to eltrombopag treatment. Eltrombopag was started at a dose of 100 mg/day (25-300). In 11 patients, dose was increased. Median dose was 150 (50- 300) mg/day. Median treatment duration was 66 (21-138) days. Eleven patients (73.3%) responded to the treatment: 9 achieved complete response (CR), and the remaining 2 achieved partial response. In the 11 responding patients, median platelet count was 18 (6-32) × 109/L vs 82 (23-173) × 109/L prior to and after treatment. Neutrophil count was 0.70 (0.05-3.9) × 109/L vs 1.75 (0.51-4.62) × 109/L. Hemoglobin was 7.08 (5-9.4) vs 9.71 (7.4-14.5) g/dL. In the 9 patients who achieved CR, the time from eltrombopag initiation to achieving CR was 39 (15-136) days; the response lasted until the last follow-up in all 9 CR subjects. Eight of 11 (72.7%) responding patients were still alive at the last follow up. There was no treatment-related mortality and no evidence thrombosis, or any other grade 3/4 toxicities.
Conclusion: These results suggest that eltrombopag is a safe and effective agent in the treatment of patients who diagnosed PGF after allo-HSCT.

P14. A CASE OF HEREDITARY HEMORRHAGIC TELANGIECTASIA WITH TREATED BEVACIZUMAB THERAPY

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OBJECTIVE: Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant disorder characterized by telangiectases of skin and mucosae and arteriovenous malformations of the lungs, liver, and central nervous system. Clinical findings are epistaxis, arteriovenous malformations and nasal mucosal bleeding. Bevacizumab, a humanized anti-VEGF antibody, is an angiogenesis inhibitor. Intravenous bevacizumab decreased severe nasal or sinus mucosal bleeding or gastrointestinal bleeding in patients with HHT.
METHODS: We presented a case with HHT treated bevacizumab therapy.
RESULTS: A case of HHT applied to clinic due to nasal mucosal bleedings and gastrointestinal bleedings in April 2015. He was 62 years old. He had no chronical disease in background. We found leukopenia and iron deficiency (WBC: 2790 mm3, hb: 8.5 gr/dl, plt: 159000 mm3). In the endoscopy, we detected widespread telangiectases in the stomach and duedonum. The patient was tretead with intravenous bevacizumab (5 mg/kg/month,12 cycles) and intravenous iron therapy. Bleedings were brought under control. The control hemoglobin level was 13.2 gr/dl. He was followed without treatment during five years. He applied with nasal mucosal bleedings and gastrointestinal bleedings again in December 2019. The least hemoglobin level was 5.6 gr/dl. We started to 4 cyles bevacizumab therapy again at the same dose. But we didn't provide the control of bleeding. The patient received many transfusions due to bleedings. We followed the patient in intensive care unit. Then, we applied to off label therapy every two weeks. Now, he is still receving bevacizumab therapy every two weeks for 4 months. The last hemoglobin is 12.0 gr/dl and there is no bleeding.
Conclusion: Introvenous bevacizumab is an efective and well tolerated therapy for patients with HHT. If the bleedings can't be controlled with using montly, the therapy should be applied every two weeks.

P15. A CASE OF MULTIPLE MYELOMA BY EXTRAMEDULLARY INVOLVOMENT IN LIVER

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OBJECTIVE: Multiple Myeloma is a plasma cell disease that accounts for approximately 17% of hematologic malignancies. The presence of plasma cells outside the bone marrow is defined as extramedullary myeloma. The rate of extramedullary myeloma is 6-20% at the time of diagnosis. **Methods:** We wanted to present a patient with multiple myeloma and extramedullary involvement in liver.
RESULTS: A case of female applied to our clinic due to hypercalcemia and anemia. She was 70 years old. She had undergone chronic kidney failure and hemodialysis for 5 months. In physical examination she was pale appearance and fatique. She had hypertension and diabetes mellitus as comorbidities. She had diverticulums in colon. We found normochrome normocytic anemia. In the laboratory tests, we detected that WBC: 9720 mm3, hemoglobin: 8.5 gr/dl, platelet: 56000 mm3, sedimentation: 21 mm /h, urea: 36 mg/dl, creatinine: 4.58 mg/dl, total protein/albümin: 50.2/33.6 g, calcium: 14.32 mg /dl, b2 mikroglobulin: 20.67. The patient was hospitalized due to malign hypercalcemia. The level of kappa light chain was 1000 mg/l, lambda light chain was 2127 mg/L. We performed bone marrow biopsy. The bone marrow was hypocelular and having 2-3% plasma cells. The patient couldn't have a PET - CT due to device problem. She received pamidronate therapy for hypercalcemia. We planned colonoscopy in terms of another reasons of malign hypercalcemia. She had undergone to an operation due to perforation during the colonoscopy. The liver biopsy was performed because of noduler lesions in liver during the operation. She was followed up in the intensive care unit after operation. We detected lambda light chain band in serum and urine immunofixation electrophoresis. The bone marrow (90%plasma cells) and liver biopsy were resulted in multiple myeloma. The patient is still receiving VCD and pamidronate therapy.
Conclusion: Liver involvement by multiple myeloma is a very rare condition at the diagnosis. We should evaluate the patients in terms of extramedullary disease at the diagnosis.

P16. RETROSPECTIVE ANALYSIS OF PATIENTS WITH CHRONIC MYELOPROLIFERATIVE NEOPLASMS

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OBJECTIVE: Chronic myeloproliferative diseases (CMPD) are clonal diseases that may cause hemostatic and thrombotic abnormalities. They progress to acute leukemia and are characterized by increases in the number of mature and immature cells in the peripheral blood as a result of uncontrolled proliferation of one or more than one type of myeloerythroid cells in the bone marrow. This study aimed to determine demographic features, incidence of Janus kinase 2 (JAK2) mutations, disease characteristics, and treatment strategies in patients diagnosed with CMPD.
METHODS: A total of 100 patients with CMPD [essential thrombocytosis (ET), n = 52; primary myelofibrosis (PMF), n = 31; and polycythemia vera (PV), n = 17] having JAK mutations admitted to outpatient clinics of Hematology Department of Sakarya University Faculty of Medicine between February 2006 and February 2013 were included with the diagnosis of BCR/ABL (The ABL gene from chromosome 9 joins to the BCR gene on chromosome 22, to form the BCR-ABL fusion gene)-negative CMPD based on the 2008 World Health Organization criteria. Age, gender, family history, secondary cancer, bleeding, history of thrombosis, whole blood cell counts, and presence of hepatomegaly, splenomegaly, and other symptoms and signs at the time of diagnosis were evaluated. Besides, a history of thrombosis and hemorrhage was assessed. The presence of JAK mutations in DNA samples was analyzed using real-time polymerase chain reaction.
RESULTS: Age and gender distribution, family history, previous incidents of bleeding, thrombosis, secondary cancer, blood hemoglobin, lactate dehydrogenase values, platelet and white blood cell counts, constitutional symptoms, minor neurologic symptoms, and presence of hepatomegaly and splenomegaly at the time of diagnosis were assessed. The incidence of JAK2 mutations was highest among patients with PMF (70.9%), followed by patients with PV (70.6%) and ET (51.9%), in this study.
Conclusion: The incidence of JAK2 mutations has offered a different perspective in BCR/ABL- negative patients with CMPD and served as an acceptable diagnostic factor. The present study had a small sample size. Hence, large-sample studies should be conducted to confirm the relationship between this mutation and CMPD.

P17. A CASE REPORT WITH RICHTER'S TRANSFORMATION

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OBJECTIVE: Richter's transformation, is an uncommon clinicopathological condition observed in about 2% to 10% of patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). Richter's transformation refers to the development of aggressive lymphoma during the course of CLL/SLL. Diffuse large B-cell lymphoma (DLBCL) occurs in the majority of cases of Richter's transformation. Clinically, patients with Richter's transformation present with an aggressive disease course with rapidly enlarging lymph nodes, hepatosplenomegaly, and elevated serum lactate dehydrogenase levels.
METHODS: We presented a case with Richter's transformation.
RESULTS: A case of female applied to our clinic with germinal center DLBCL. She was 71 years old. She had undergone total gastrectomy operation because of perforation. She had no chronic disease in background. Clinic findings were nausea, vomiting and lack of appetite. We found that in laboratory tests: Wbc: 12.68 K/uL, Neutrophil: 8570 K/uL, Lymphocyte: 2.66 K/uL, Hgb: 13. 7 g/dL, Plt: 903 K/uL, sedimentation: 75 mm/h, creatinine: 0.78 mg/dL, AST: 11 IU/L, ALT: 6 IU/L, LDH: 637 U/L, Crp: 0.862 mg/dL, B2 microglobulin: 3.93 mg/L at the diagnosis. We planned PET-CT scan to detect stage of disease. Bone marrow biopsy was also performed at the same time PET-CT. The result of bone marrow aspiration was 10% lymphoid cell infiltration and biopsy was CLL/SLL. The patient was evaluated as stage 4 A lymphoma according to the Ann Arbor staging system and IPI (International prognostic index) score was 3. She probably had CLL/SLL but it was unknown to till bone marrow evaluation. She was treated with RCHOP chemotherapy. After first cycle, 25% dose reduction was achieved because of deep neutropenia. She only received 3 cycle of RCHOP. She was followed in intensive care unit due to septic shock and she died three monts later after diagnosis.
Conclusion: Richter's transformation is a serious complication of CLL/SLL. The clinical course is very aggresive, low response and poor prognosis with the currently available chemotherapeutic regimens. It is mostly mortal.

P18. HIGH-GRADE B-CELL LYMPHOMA IN A PATIENT PREVIOUSLY TREATED FOR HODGKIN LYMPHOMA: A CASE REPORT

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OBJECTIVE: High Grade B-cell Lymphomas (HGBL) have been defined as a new separate entity in 2016 revised WHO classification of lymphoid neoplasms. The previously well-known Double- and Triple-Hit Lymphomas (DHL/THL) are included in this umbrella category under the name of HGBL with MYC and BCL2 and/or BCL6 rearrangements. According to studies, the incidence of diffuse large B cell lymphoma (DLBCL) in the United States and England, is approximately 7 cases per 100,000 persons per year. In Europe as a whole, the incidence is approximately 4.92 cases per 100,000 persons per year. Unfortunately, the incidence of HGBL is unknown accurately. High-grade B-cell lymphoma after therapy of Hodgkin lymphoma is an extremely rare condition. In this report, we aimed to present a rare case with HGBL after treatment of Hodgkin lymphoma (HL)

METHODS:

RESULTS: A 51 year-old male patient presented with abdominal pain. He had no fewer, diarrhea or constipation. Organomegaly was not detected. A 2 x2 cm mass palpated right to the umbilicus. Number of leukocytes was 6730/µL, lymphocytes was 1500/µL. His hemoglobin level was 10,1 g/dL. He was diagnosed with Mixed cellularity classical Hodgkin lymphoma (2004) his ann arbor stage was 3. he was treated with doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD chemotherapy regimen). After 6 cycles of ABVD, there is no sign of lymphoma in positron emission tomography/computed tomography (PET/CT). He was followed in complete remission during 16 years until 3 months ago. He was checked for abdominal pain and CT scan showed that he had multiple lymphadenopathies (LAPs) in right paratracheal region and mass lesion in the form of aneurysmatic dilatation in the lower right quadrant with asymmetric wall thickening on the ileal ans, he had multiple LAPs in the periphery of this mass. Patient underwent excisional biopsy from that mass with an initial diagnosis of Hodgkin disease. Immunohistochemical studies of resected tissue showed diffuse infiltration of CD10, CD20 and CD38 positive neoplastic medium lymphoid cells with an high mitotic index. c-myc and Bcl-6 were positive. The Ki67 proliferation index was%98. According to the results of the immunohistochemical examination, when the Hans algorithm was applied, the findings were found to be compatible with the germinal center origin (GCB) B cell phenotype. In the infiltration consisting of medium-sized cells with a high mitotic index, immunophenotypic properties were also compatible with Burkitt's lymphoma. The diagnosis was high grade B-cell lymphoma. He was admitted and treated with Cyclophosphamide, vincristine, doxorubicin, dexamethasone, rituximab (Hyper-Cvad chemotherapy regimen).

CONCLUSION: HGBL after therapy of HL is an extremely rare condition. HGBL can occur primarily and incidentally or may be secondary to chemotherapeutic agents previously used. Although first hematologic malignancy was totally cured, our patients monitoring must continue regularly. Also more studies are needed to learn about the long-term effects of the chemotherapeutic agents used.

P19. TRANSFORMED NON HODGKIN LYMPHOMA AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION IN RELAPSED/ REFRACTORY HL: A CASE REPORT

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OBJECTIVE: Lymphoma is a malignancy that is the most seen including our immune system. It is divided into two categories: Hodgkin (HL) and Non-Hodgkin Lymphoma (NHL), according to their clinical signs, location that expected where originating from the body, morphology, cytopathology, patterns of malign cells behavior and treatment algorithms. Factors developing HL and NHL are some of hereditary and acquired immune system deficiency related diseases or genomic abnormalities, occupational and environmental exposures and infectious agents like some viruses, bacterias, parasites. In this case we aim to explain these two types of diseases will be able turn into each other.

METHODS:

RESULTS: A 38 year old man presented weakness, weight loss and fever (2006). In his family history, his all four siblings were diagnosed HL, two of them were died due to HL. He diagnosed mixt-celluler HL with cervical lymph node biopsy. His ann-arbor stage was 3 B at the time of diagnosis. Human immunodeficiency virus is negative. EBV-VCA Ig G and Anti-EBNA were positive. He was treated with doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD chemotherapy regimen) for six cycles. He was in complete remission during four years. Because of mediastinal progression was detected on his control PET-CT scan, he was treated autolog stem cell transplantation (2010) after two times ICE protocol for first relapsed disease. In post-transplant period, he was also given radiation therapy on mediastinal side. A new lymphadenopathy was determined on his control examinations and he described the B symptoms again. In excisional lymph node biopsy from his inguinal region reported as lymphocyte-rich classic HL which is EBV-LMP1 positive on Reed-Sternberg cells on immunohistochemical analysis (2014). Brentuximab vedotin and Bendamustine combined chemotherapy was given to the patient for second relaps every 28 days during 6 cycles. He was treated only Brentiksumab after the sixth cure and totally completed to thirty one cycle. On the twenty night cycle of the therapy, hypermetabolic some regions and hyperdense nodular formations on jejunal loops was detected on his control positron emission tomography. Upper and lower gastrointestinal tract endoscopia were performed and the biopsy from ileum was resulted mucosal infiltrations consisting of atypical cells with a large number of mitosis, diffuse large cell lymphoma. He was treated with 2 cycles of R-ICE regimen as a salvage chemotherapy. The last PET-CT (2020) scan and bone marrow biopsy were evaluated in favor of stable disease. The patient refused to proceed allogeneic stem cell transplantation.

CONCLUSION: Lymphomas contain so many different subgroups in itselfs and analyze which of them is the main diagnosis is supported by pathologic, immunochemical and genetic methods. But some of ethiological factors like viral load and effects of our immune system is poorly understood. Transforming of these diseases seems to be related with EBV reactivation in immuncompromised patient on a period of T-cell suppression by disrupting interaction between the T and B lymphocytes or otoactivation of B lymphocytes. Both of chemotherapy agents and radiotherapy may trigger the variations on this interactions in a way that we do not know yet.

P20. TOCILIZUMAB IS A CHOICE FOR STEROID REFRACTORY GI TRACT GVHD TREATMENT: A CASE REPORT

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OBJECTIVE: Acute graft-versus-host disease (GVHD) is a common complication of allogeneic stem cell transplant (ASCT) that classically presents in the early post-transplantation period. GVHD is a complicated clinical syndrome involving a severe immune reaction mediated by immunologically competent cells, mainly T lymphocytes resulting in organ dysfunction. The skin, gastrointestinal tract, and liver are the principal target organs in patients with acute GVHD.
METHODS:
RESULTS:: A 54 -year-old male patient is that diagnosed with transformed acute myeloid leukemia (AML) from myelodysplastic syndrome (MDS) was done fully compatible allogenic stem cell transplant with CyBu (Cyclophosphamide-mesna-busulfan-defibrotide-cyclosporine-methotrexate) conditioning regimen. Patient was admitted with diarrhea (15-20 times in a day), nausea, vomıtıng, impaired oral intake after 75 days of the transplant. On his physical examination; he had wide spread, red colored macules and tenderness in abdomen. In laboratory analysis; AST/ALT:<5/8 U/L, ALP/GGT: 73/74 U/L, T. bil/d. bil: 0,84/0,49 mg/d Land bone marrow biopsy was performed and he was in complete remission. Patient underwent rectosigmoidoscopy and excitional biopsy from skin with an initial diagnosis of acute GVHD and acute skin and gastrointestinal (GI) tract GVHD was confirmed with histopathological findings. The treatment started with glucocorticoid 2 mg/kg/day and cyclosporine 2 x2 mg/kg/day. On the patient's monitoring liver enzymes and bilirubine progressed and the clinical findings especially diarrhea did not improved. Etanercept treatment was started for the patient who didn't benefit from steroids and cyclosporine. Although the skin GVHD was improved 25 mg sc etanercept therapy 2 times in a week for 4 weeks, GI tract GVHD did not get better. The patient who did not benefit from this treatment was given tocilizumab 480 mg every other week for 2 cycle and the frequency of diarrhea was decreased to 2-3 times in a day.
CONCLUSION: Acute GVHD is one of the most mortal complications after ASCT. Clinically significant acute GVHD occurs in 9 to 50 percent of patients who receive an ASCT. İmmunosuppressive agents such as cyclosporine, glucocorticoide, mycophenolate mofetil, antithymocyte globulin, methotrexate are used for prophylaxis of acute GVHD. Although treatment of acute GVHD included cyclosporine and steroid at first step, there is no well known therapy for further line. Nevertheless, ruxolutinib is a recommended agent rather than other immunosuppressive agents; it is a debate for GI tract GVHD due to using by orally. Tocilizumab would be better option for these patients because of using intravenously.

P21. IMID RETREATMENT IN PATIENTS REFRACTORY TO BOTH AN IMID AND AN ANTI-CD38 ANTIBODY INDUCES SIGNIFICANT RESPONSE RATES POST ANTI-CD38 EXPOSURE

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OBJECTIVE: The survival of myeloma patients has doubled the past decade, however, patients refractory to both proteasome inhibitors (PIs) and immunomodulatory drugs (IMiDs) still have poor prognosis. Immunotherapy with monoclonal antibodies targeting cell-surface antigens is a promising treatment strategy with different mechanisms of action. The combination of daratumumab, pomalidomide and dexamethasone (DaraPomDex) has demonstrated significant activity even in patients refractory to both drugs and a potential mechanism may be re-sensitization to pomalidomide. Another report showed that daratumumab-refractory patients who previously failed IMiD, responded when the IMiD was added to daratumumab. This provided a proof of principle that anti-CD38 antibodies can alter the underlying pathophysiology, and can potentially overcome refractoriness to IMIDs. Increased CD38 expression after IMiD exposure could be a mechanism of IMiD resistance, and anti-CD38 agents may act by eliminating this effect. Another potential mechanism could involve the reemergence of IMiD-sensitive clones after an IMiD-free period. There is data that daratumumab alters the tumor immune microenvironment, and this effect may be long lasting, even after daratumumab discontinuation. The aim of the study was to evaluate the efficacy of re-treatment with IMiD-based therapy in patients refractory both to IMiDs and anti-CD38 antibodies.
Methods: The study included 38 patients who were refractory to antiCD-38-based therapy and to at least one IMiD. Overall, 26 (68%) patients had received lenalidomide, 11 (29%) pomalidomide and 1 (3%) thalidomide before anti-CD38 treatment
RESULTS: Median number of prior lines before IMiD retreatment was 4 (range 2 to 13). Overall, 4 (11%) patients received lenalidomide-, 33 (86.5%) pomalidomide-, and 1 (2.5%) thalidomide-based regimens post anti-CD38. The majority of patients were treated with pomalidomide-cyclophosphamide-dexamethasone (PCD) (n=13) and pomalidomide-dexamethasone (PomD) (n=11). The remaining 14 patients were treated with other IMiD-based triplets. Importantly, 10 (26%) patients received the same IMiD as prior to anti-CD38 exposure (lenalidomide n=2, pomalidomide n=8). Median time from diagnosis to IMiD re-treatment was 61.5 months. Overall, 20 patients (53%) achieved a response during IMiD retreatment, including CR=1, VGPR=5, PR=10 and MR=4; 11 patients achieved SD, whereas 7 patients progressed. The disease control rate (DCR=SD+PR+VGPR+CR) was 82%. Among the patients re-exposed to the same IMiD, 5 responded, 3 progressed and 2 remained stable. 79% (22/28) of the patients received pomalidomide following previous exposure to lenalidomide; among them, 15/22 (68%) patients responded, 3 remained stable and 4 progressed. Interestingly, 10 out of 13 (77%) patients who received PCD responded. Median PFS for all patients was 4 months (range 2.9-4.8). Median time to next treatment (TtNT) for the whole study cohort as well as for those who received the same IMiD pre- and post-exposure to anti-CD38 was 4.2 months as well. Median duration of response (DoR) for the responders was 7 months. Median OS 5.3 range 0.5-35.5.
CONCLUSION: IMiD retreatment in patients refractory to an IMiD and an anti-CD38 antibody can induce significant response rates, even among patients re-exposed to the same IMiD. This indicates that after anti-CD38 therapy a long lasting, probably immunomodulatory effect may be associated with some degree of re-sensitization to IMiDs.

P22. PATIENTS WITH ASYMPTOMATIC MULTIPLE MYELOMA WHO PROGRESS ONLY WITH BONE DISEASE DETECTED IN WHOLE BODY LOW DOSE CT-A PROSPECTIVE STUDY IN 100 PATIENTS

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OBJECTIVE: Smoldering MM (SMM) is an intermediate clinical entity between MGUS and MM, with a risk of progression to symptomatic disease at 10% per year. Bone disease is the most frequent related symptom of MM, with approximately 90% of patients developing bone lesions throughout their disease course. Therefore, imaging plays a crucial role in diagnosis and management of these patients. The purpose of this study was to evaluate the role of WBLDCT in the early identification of patients with asymptomatic MM who progress with bone disease only and who require immediate antimyeloma treatment.

METHODS: Our study was approved by the local IRB and all patients provided informed consent. All patients diagnosed with SMM based on the 2003 International Myeloma Working Group (IMWG) definition of SMM were serially assessed with WBLDCT from July 2013 until March 2020 as part of our institutional workup. The assessments were performed at baseline, 1-year post diagnosis and every 1 year thereafter. The patients enrolled in the study were those who had at least 2 consecutive CT assessments at the above described time points. All WBLDCT exams were performed with a 16-detector CT scanner. The CTs were evaluated by two experienced radiologists, blinded to the clinical and laboratory data.

RESULTS: We prospectively evaluated 100 patients with SMM (median age at diagnosis 61 years, range 40-86 years, 52 female /48 male) who underwent WBLDCT at the above described time points. Median number of WBLDCTs exams performed was 2.5 (range 2-5). Totally, 31 patients progressed (either with CRAB criteria and/or at least one myeloma defining event). During a median follow up of 57 months 31 patients have progressed (with either CRAB criteria and/or at least one myeloma defininf event). Importantly, 10 of 31 patients progressed only with bone lesions that were identified on the scheduled WBLDCT as per protocol. Median time to progression from asymptomatic to symptomatic disease for all patients has not been reached, while median time for those who actually progressed was 22 months (95% CI: 15,6-28,4). For the subgroup of patients who progressed with bone lesions only the median time was also 22 months (95%CI: 3,4-40,6). Median time to progression was not statistically different between the two progressor subgroups. All patients were initiated with antimyeloma treatment immediately post evolution to symptomatic disease. PFS for all 31 patients at first line treatment was 52 months (95%CI: 34,5-69,5) and median PFS for bone progressors has not yet been reached. Among the patients who progressed 29 were alive at the time of the analysis. The 2 deaths that occurred were one related (progressive disease) and one unrelated to multiple myeloma (cardiovascular event). Neither had progressed with isolated bone involvement.

Conclusion: In conclusion, our strategy allowed early detection of bone lesions in 10% of our patients and these patients were immediately initiated with antimyeloma treatment to avoid further myeloma-related complications. Consecutive low-dose WBLDCT studies can identify early myeloma evolution to symptomatic disease and optimize the disease monitoring along with our therapeutic strategy.

P23. ALLOGENEIC STEM CELL TRANSPLANTATION WITH BUSULFAN-FLUDARABINE-THIOTEPA CONDITIONING REGIMEN FOR THE PATIENT WITH SECONDARY CNS INVOLVEMENT OF DIFFUSE LARGE B CELL LYMPHOMA

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OBJECTIVE: Systemic non-Hodgkin lymphoma (NHL) can involve the nervous system at every level. The majority of cases of secondary CNS lymphoma derive from histologically high-grade systemic lymphomas such as diffuse large B cell lymphoma (DLBCL) or Burkitt lymphoma. Secondary CNS involvement (SCNS) is a profoundly adverse complication of DLBCL. Evidence from older series indicated a median overall survival (OS) <6 months; however, data from the immunochemotherapy era are limited. In this report, we present a patient with secondary CNS involvement by diffuse large b cell lymphoma who is treated with Allogeneic stem cell transplantation (AlloSCT) successfully after autologous stem cell transplantation (autoSCT) failure.

METHODS:

RESULTS: 25 years old male patient was admitted with lower back pain and fever. After generalized lymphadenopathy and kidney lesions are noticed on computerized tomography (CT) scan, a kidney biopsy was performed and the patient is diagnosed with DLBCL. After 6-course of rituximab-cyclophospamid-doxorubicin-vincristine-prednizolon (R-CHOP regimen), secondary brain infiltration was noticed. He was treated with Rituximab-idarubicin-cytarabine-methotrexate (R-IDARAM regimen) chemotherapy and after 2 cycles of R-IDARAM regimen, an enlargement of the cranial lesion was seen on CT scan. Intrathecal therapy and radiotherapy were performed. Afterwards the patient received TECAM conditioning regimen, an autoSCT was done. 2 months later, a control MRI reveals an enlargement of the cranial lesion and the patient receives another 21 sessions of radiotherapy. After the radiotherapy, because of the lungs infiltration and the progression of the cranial lesion, 2 courses of rituximab-methotrexate-cytarabine (Hyper-CVAD) chemotherapy was given and he achieved partial remission and proceed to alloSCT from his full matched sibling donor with Busulfan-thiotepa-fludarabine preparation regimen successfully. Neutrophil engraftment occurred 18 days after the transplantation and platelet engraftment occurred 21 days after the transplant. He is still in partial remission after 2 months from alloSCT.

CONCLUSION: Patients who have disease progression following the use of autoSCT generally have a poor prognosis. If such patients are fit and can undergo alloSCT, a proportion of patients may achieve durable disease control, particularly those patients, who have good performance status, prolonged remission duration with autoSCT, and disease remission at the time of alloSCT. AlloSCT for lymphoma is usually considered in the salvage setting, as an alternative to autoSCT or after failure of autoSCT. Retrospective studies demonstrate that busulfan/cyclophosphamide and cyclophosphamide/TBI are frequently used myeloablative regimens for alloSCT. However, thiotepa based conditioning regimen would be a good choice for the patients with CNS lymphomas, the optimal conditioning regimen with alloSCT for NHL has not been tested yet in a randomized trial.

P24. SUCCESSFULL AUTOLOGOUS STEM CELL TRANSPLANTATION FOR POEMS SYNDROME: A CASE REPORT

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OBJECTIVE: POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, Skin changes) is a rare condition characterized by the presence of a monoclonal plasma cell disorder and peripheral neuropathy, along with other systemic symptoms. The International Myeloma Working Group (IMGW) criteria for diagnosis for POEMS requires the presence of at least three major criteria (i.e, polyneuropathy plus monoclonal plasma cell disorder plus any one of the following three: osteosclerotic bone lesion, Castleman disease, or elevated serum or plasma vascular endothelial growth factor (VEGF) levels), along with the presence of at least one of the six minor criteria (Organomegaly, Extravascular volume overload, Endocrinopathy, Skin changes, Papilledema, Thrombocytosis/polycythemia). The absence of either osteosclerotic myeloma or Castleman disease should make the diagnosis of POEMS syndrome suspect. There is no standard treatment for POEMS syndrome. Radiation therapy is appropriate option for those with limited disease (one to three isolated bone lesions), and chemotherapy similar to multiple myeloma for those with widespread bone lesions. Autologous stem cell transplantation (ASCT) with Melphalan is an option for patients with rapidly progressive neuropathy and for younger patients with widespread osteosclerotic lesions.
Methods: ASCT with melphalan as a conditioning regimen
RESULTS: 62 years old man who has a history of Celiac disease evaluated for 3 months of mononeuropathy multiplex,1 month of diabetes insipidus and 1 month of vasculitic rash. On physical examination, there was clearly weakness of lower limbs. He has mononeuropathy multiplex in Electromyelography (EMG). Multiple myeloma was reported as IgG kappa monoclonal, CD 138 positive plasma cells reaching up to 40% in his bone marrow biopsy in Agust 2018. Also Diabetes insipitus was detected. The patient with Polyneuropathy, monoclonal plasma cell disorder, endocrinopathy, skin changes was diagnosed POEMS. Bortezomib, Cyclophosphamid, Dexamethason therapy (VCD regimen) was started in September 2018. After 5 cycles of VCD, the patient was mobilized with G CSF. ASCT with melphalan as a conditioning regimen was performed and he was engrafted successfully on the 20 th day of the transplant. He was in complete remission for 2 years after ASCT. Neuropathy findings began to improve after ASCT and he has no complain about neuropathy any more.
CONCLUSION: POEMS syndrome is a rare, chronic, multisystemic, paraneoplastic syndrome. Although the pathophysiology of POEMS syndrome is not fully known, the source of its symptoms is thought to be excessive VEGF production by neoplastic cells. VEGF may also use the increase for diagnostic purposes. Also similar to chronic inflammatory demyelinating polyneuropathy (CIDP) with its clinical and laboratory features. Patients diagnosed with CIDP should be examined in terms of possible gammopathy and M protein and bone lesions should be investigated. As in our patient, widespread osteosclerotic lesions and bone marrow involvement on bone marrow aspirate and biopsy has been treated ASCT after Bortezomib-based therapy.

P25. INVOLVEMENT OF CENTRAL NERVOUS SYSTEM WITH INVASIVE FUNGAL INFECTION CAUSED BY SAPROCHAETE CLAVATA IN A PATIENT WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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OBJECTIVE: Infections are the most important cause of mortality and morbidity during the treatment of adult acute leukemia. Opportunistic rare fungal infections might be seen in spite of all efforts to prevent fungal infection in leukemia patients. Saprochaeta clavata (SC), formerly called Geotrichum clavatum, is a filamentous yeast-like fungus that has recently been reported as an emerging opportunistic pathogen mostly in acute leukemia patients. Here, we report a patient with B cell acute lymphoblastic leukemia (B-ALL) who had severe fungal infection caused by SC that involved to central nervous system during his induction chemotherapy.
METHODS: Case.
RESULTS: A 50-year-old male patient, who admitted to our department with pancytopenia, was diagnosed B-ALL by bone marrow aspiration and biopsy findings. HyperCVAD chemotherapy regimen was started concomitantly with prophylaxis against infectious agents such as bacterial (levofloxacin), PCP (trimethoprim-sulfamethoxazole), viral (valaciclovir), and fungal (micafungin). On chemotherapy day 11, the patient had cough, shortness of breathe, and fever. There was no any findings to show infection area on physical examination. Blood, catheter, and urine cultures were sent to laboratory. Chest CT did not reveal any abnormality. The patient with febrile neutropenia was started to treat by piperacilin-tazobactam and vancomisin. On the third day of antibiotherapy, oral mucositis and diarrhea occurred accompanied with persistent fever. Day after, left hemiparesis and impaired consciousness developed in the patient. Brain CT showed hypodense areas in the bilateral periventricular area, located in the basal ganglia loj, 2 x3 cm in size on the right and 2 x1.5 cm in size on the left, respectively. Diffusion restricting areas were detected in bilateral basal ganglia, thalamus, cerebral and cerebellar hemispheres in whole brain MRI. In addition to those radiologic findings, both blood and catheter culture results which had been taken during first febrile period showed SC and galactomannan test was positive as well. The cultures were repeated and micafungin was switched to voricanazole. Infective endocarditis was excluded and he was sent to intensive care unit (ICU) for close follow-up. Unfortunately, the patient was intubated due to respiratory distress and renal failure which developed during the ICU period. In the meantime, three other blood culture results were compatible with SC. At the 20 th day of his treatment, the patient passed away because of fungemia that spread out to central nervous system.
CONCLUSION: Acute leukemias especially acute myeloid leukemia are high-risk diseases for fungal infections. Using prophylaxis to prevent fungal infection, early diagnosis, starting immediate and appropriate therapy are milestones for treatment of fungal infection and at the same time prognosis of patients with acute leukemia. SC might cause hepatosplenic abscess, multiorgan failure and respiratory distress. More rarely, it can spread out like mass formation that we can see only in one case in the literature as shown in our case as well. Though, it is difficult to document the infection, culture is important for diagnosis as shown in our case. The optimal treatment of SC whose resistant to echinocandins is not yet clear. Unfortunately, 60-80% mortality rate has been reported in patients with hematological malignancies.

P26. BELINOSTAT FOR THE RELAPSED REFRACTORY PERIPHERAL T CELL LYMPHOMA: A CASE REPORT

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OBJECTIVE: Peripheral T-cell lymphomas (PTCLs) are one of heterogeneous group of non Hodgkin lymphomas with a poor prognosis. Anthracycline-based regimens with or without etoposide are used widely as a first line therapy but unfortunately these regimens could not improve the outcomes. Although new agents (pralatrexate, romidepsin, brentuximab vedotin) are started to use for treatment of PTCL in recent years, patients with PTCL still experience relapse. Histone deacetylase (HDAC) inhibitors, vorinostat, romidepsin and, recently, belinostat have proven effective for the treatment of relapsed/refractory PTCL.
METHODS: Herein, we reported the patient who has replapsed refractory angioimmunoblastic T-cell lymphoma (AITCL) treated with belinostat successfully. According to our knowledge this is the first experience of belinostat in Turkey.
RESULTS: In 2017, a 63 year old female patient diagnosed with AITCL from axillary lymph node biopsy. AITCL infiltration was shown in bone marrow biopsy. Positron emussion tomography (PET) was performed and Ann Arbor stage was 4. She has a history of by-pass surgery and osteoporosis. Following 6 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone therapy (CHOP-21 regimen), she achieved partial remission with no lymphoma clue on PET scan but disease was stable in bone marrow infiltration. She was hospitalized for salvage regimen and autologous stem cell transplantation but first cycle of ifosfamide, etoposide, carboplatine (ICE regimen) she was entubated due to fungal pneumonia. After discharged fromintensive care unit, she refused to transplantation procedure. Brentuximab vedotin (BV) was started and the disease was progressed from lymph nodes after 5 cycles of BV. The treatment was changed to pralatrexate and she had relapsed again after 4 cycles of prolatrexate. She was treated with lenalidomide for 2 months but she could not tolerate lenalidomide due to skin rash and gave up. After 5 line prior therapy, belinostat was started (february 2020), target dose 1,000 mg/m2 day 1 to 5 in a 21 day cycle. It was well tolerated and after 2 cycles of belinostat therapy, bone marrow biopsy and pet scan were showed that she achieved complete response. She has been in complete remission for 6 months.
Conclusion: Although new agents are promising for patients with relapsed or refractory PTCL, with response rates of 29% (pralatrexate) and 25% (romidepsin). Most of the patients like our case usually relaps in a short time. The BELIEF study has established that belinostat produces a meaningful overall response rate of approximately 26%, with complete remission rate of 11% with minimal toxicities and belinostat is promissing durable response for relapsed refractory PTCL.

P27. DIFFUSE PATTERN FOLLICULAR LYMPHOMA WITH CD23 CO-EXPRESSION: EVALUATION OF SIX CASES

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OBJECTIVE: Diffuse growth pattern dominancy and CD23 co-expression is very rare for follicular lymphoma (FL) and may cause diagnosis difficulties. In 2009, single case series was published and diffuse pattern follicular lymphoma was well-defined. This type of FL is characterized with CD23 co-expression, lack of t (14; 18) IGH/BCL2 translocation and presence of 1 p36 deletion. In this report, we aim to evaluate the patients with diffuse pattern FL from diagnosis to treatment.
METHODS: Six patients who were diagnosed with diffuse pattern FL between 2012-2020 in Ege University, School of Medicine, Department of Hematology were evaluated, retrospectively. Age, gender, immunohistochemistry staining, Ki67 level, the lymph node of diagnosis, complete blood count, biochemical parameters, FLIPI scores, stage and grade of the disease, treatments and response to the therapy were screened.
RESULTS: Six patients were evaluated and all of the patients biopsy specimens were positive for bcl-6, CD10, CD20, weak positive or negative for bcl-2 and showed CD23 co-expression by immunohistochemistry and were diagnosed as diffuse pattern FL. The median age at diagnosis was 54. All of the patients were diagnosed from an inguinal lymph node. 4 patients had stage 2 and 4 patients had grade 1 A disease while only one patient had grade 4 disease with bone marrow involvement. Median Ki-67 value was 25%. FLIPI score of 4 patients were 0, while one patient's score was 3. The oldest patient had stage 2 and grade 4 disease with Ki67 30%, treated with R-CVP regimen as a systemic chemotherapy because of extensive involvement and B symptoms and achieved complete remission. One patient with grade 1 and bulky disease was also treated with R-CHOP as a systemic chemotherapy, localized RT and rituximab maintenance for two years achieved complete remission. 4 patients who had grade 1 A localised disease and the only region which involved was inguinal lymph nodes were treated with localized radiotherapy, and three of them were treated successfully and followed up in remission. To one patient who was treated with radiotherapy to inguinal lymph node had stable disease after treatment, re-biopsy performed to the rest inguinal node and diagnosis was confirmed and followed-up without treatment. 5 of 6 patients are still followed up without progression and one patient died two years after the therapy with unrelated reason of lymphoma.
CONCLUSION: FL is the most frequent form of Non-Hodgkin Lymphoma and is a rare entity. Predominantly diffuse FLs have been accepted as an entity in the WHO classification and characterized by diffuse growth pattern of centrocytes and centroblasts. The presence of diffuse pattern and lack of t (14: 18) should guide the clinician to diffuse pattern FL and CD23 should stain. Chromosomal alterations such as 1 p36 should search. Due to the infrequency, the prognosis is not fully determined but estimates as intermediate. Diffuse FL has characteristic well-defined clinical features. Tumor is mostly large and confined to the inguinal region and patients follow especially indolent clinical course and can be treated with localized therapy such as radiotherapy. Cases in our study highlights a unique and difficult diagnosis of an uncommon subtype of FL.

P28. RETROSPECTIVE EVALUATION OF VON WILLEBRAND DISEASE: A SINGLE CENTER EXPERIENCE

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OBJECTIVE: Von Willebrand disease (VWD) is the most common inherited bleeding disorder due to the qualitative or quantitative defect of Von Willebrand Faktor (VWF). VWD has an autosomal pattern and platelet adhesion or aggregation is detective. The diagnosis based on a personal or family history of bleeding and laboratory tests of VWF or/and factor 8. The most common symptoms are ecchymosis, menorrhalgia, mucosal bleeding and bleeding from minor wounds. Most patients are diagnosed with bleeding after small surgery or dental procedures. The prevalence of disease is 1% while only 10% of VWD patients are symptomatic. The aim of the study is to detect bleeding pattern and frequency of bleeding in patients with VWD in our center.
METHODS: 125 patients were evaluated who were diagnosed between 2013-2020 at Ege Adult Hemophilia and Thrombosis Center between 2013-2020, retrospectively. Age, gender, type of VWD, bleeding type, localisation and treatments were screened for each patient.
RESULTS: 125 VWD patients were screened. The median age of the patients was 33,2 (range 19-73). The patients were composed 98 (78,4%) females, 27 (21,6%) males. 32% of patients are type 1, 20% are type 2, 24%are type 3 and 24%are low VWD. Bleeding patterns were evaluated separately. The most common bleeding pattern was mucosal bleedings. 60.8% of patients had mucosal bleeding at their life-span at least once, 29,6% had ecchymosis and 13.5% had intraarticular bleeding. Patients were divided into three group to evaluate bleeding frequency and location. We observed that 19.2% patients had more than three different bleeding location as mucosal (nose or dental bleeding, menorrhalgia, gastrointestinal bleeding etc.) or joint bleeding. 11,2% of patients were asymptomatic at the diagnosis. 70.4% of female patients had menorrhalgia. 58.4% of patients were treated with factor replacement therapy were under on-demand factor treatment and only 6 patients were followed up under factor-prophylaxis. Patients were treated with factor replacement therapy, desmopressin or transamine during bleeding. The ratio of therapies were 40%, 12.8%, 57,6%, respectively.
Conclusion: VWD is the most common inherited disorder of hemostasis and comprises of heterogeneous subtypes. VWD has various genetic, clinical and laboratory findings and due to incomplete penetrance and mild deficiency of VWF, some patients remain asymptomatic while some patients have several bleeding. Despite of increasing knowledge and insights into diagnosis and management of VWD, still several issues and questions remain and need to be enlightened especially for diagnosing and treating patients with serious and life-threating bleeding.

P29. EXPRESSION OF THE NOVEL TUMOR SUPPRESSOR SAMHD1 BY HODGKIN-REED-STERNBERG (HRS) CELLS IS AN INDEPENDENT, ADVERSE PROGNOSTIC FACTOR IN CLASSICAL HODGKIN LYMPHOMA (CHL)

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OBJECTIVE: The SAM domain and HD domain 1 (SAMHD1) protein is a deoxynucleoside triphosphate (dNTP) triphosphohydrolase, which has been initially described to restrict human immunodeficiency virus type 1 (HIV-1) in the immune cells through depletion of intracellular dNTP substrates required for HIV-1 replication. Mutations of SAMHD1 gene have been linked to Aicardi-Goutières syndrome (AGS) and have been detected in a subset of CLL and -prolymphocytic leukemias resulting in decreased mRNA levels. Therefore, SAMHD1 may play a role in oncogenesis as a tumor suppressor. In addition, SAMHD1 may confer resistance to nucleoside-based chemotherapies such as cytarabine by hydrolysing their active triphosphate metabolites and its high protein levels correlate with poorer clinical outcome in acute myeloid leukemia. SAMHD1 seems to be downregulated in the neoplastic HRS cells of cHL (Xagoraris et al, Blood 2017; 130: 1480, abstract), however, its prognostic significance is not yet established.

METHODS: The study cohort included 154 patients of HL (98 males, 56 females) with a median age 37 years (14-93), Ann Arbor stage (AAS) I/IIA in 56% and B-symptoms in 34%. Treatment was ABVD or equivalent regimens in 75% of the 125 patients with available data. Histologic subtype was nodular sclerosis in 59%, mixed cellularity in 29%, lymphocyte-rich in 2%, lymphocyte-depleted/unclassifiable cHL in 4%, whereas 6% of cases had nodular lymphocyte predominant HL and were also included. SAMHD1 expression was assessed by immunohistochemistry using diagnostic lymph node biopsies obtained prior to treatment and a monoclonal antibody (Bethyl Laboratories, San Antonio, TX). A double immunostaining (SAMHD1/CD68) assay was also utilised since CD68+ histiocytes are strongly positive for SAMHD1 and were distinguished from the HRS. The percentage of SAMHD1-positive cells was calculated by counting at least 500 tumor cells in each case. Freedom from progression (FFP), overall survival (OS), and disease-specific survival (DSS) were the clinical endpoints.

RESULTS: Using a 20% cutoff, SAMHD was positive in 48 of 154 (31.2%) patients. SAMHD1 expression as not significantly associated with age, gender, AAS, B-symptoms, anemia or histologic subtype. In 125 patients with compete survival data and median follow up of 90 months (7-401 months), SAMHD1 expression significantly correlated with inferior FFP at 10 years (70% vs 51% for SAMHD1 <20% and ≥20%, p=0.025). Similarly, 10-year OS was 86% (p=0.01) and 10-year DSS was 92% vs 72% (p=0.013). In multivariate analysis ≥20% SAMHD1 expression was independently associated with worse FFP (p=0.005) along with advanced AAS (IIB, III, IV) (p=0.044), NS histology (p=0.007) and treatment without anthracycline (p=0.037). The association of SAMHD1 ex-

pression with OS and DSS was significant and independent of other factors as well, with age and treatment without anthracycline contributing additional prognostic information for these endpoints.

CONCLUSION: SAMHD1 is expressed by the HRS cells in approximately one third of HL patients and is independently associated with adverse clinical outcomes. These findings may have therapeutic implications since SAMHD1 inhibitors are under investigation for clinical use.

P30. DEVELOPMENT OF CLASSICAL HODGKIN LYMPHOMA AFTER SUCCESSFUL TREATMENT OF PRIMARY MEDIASTINAL LARGE B-CELL LYMPHOMA: RESULTS FROM A WELL-DEFINED DATABASE

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OBJECTIVE: Classical Hodgkin Lymphoma (cHL) and Primary Mediastinal Large B- Cell Lymphoma (PMLBCL) have been widely studied as separate entities but are poorly covered as metachronous pathologies in the literature. Only seven cases of cHL following PMLBCL have been described so far. Interestingly, there are no data on the cumulative incidence (CI) and potential risk factors for this very rare event. Our aim was to evaluate the frequency of this rare occurrence in the Greek population of patients with PMLBCL as well as to identify specific clinical and treatment data associated with this outcome based on the analysis of a well- defined database.

METHODS: We searched our database of PMLB|CL patients treated in the era of rituximab for the occurrence of sequential cHL over the period 2001-2020. Sequential (metachronous) cHL lymphoma was defined as the development of cHL following the initial diagnosis of PMLBCL. All the identified cases had been reviewed at the time of cHL occurrence and both the diagnosis of PMLBCL and cHL had been confirmed by expert hematopathologists.

RESULTS: The database included 433 patients with PMLBCL treated in the rituximab era with R-CHOP or similar regimens (n=348) or R-DA-EPOCH (n=85). After a median follow-up of 45 months, we identified three cases of cHL; two patients were males and one female aged 26, 27 and 27 years old at PMLBCL diagnosis and all had mediastinal stage I disease. Initial treatment

was R-CHOP without RT. All three patients developed cHL at 4.3, 6.6, and 9.8 years from PMLBCL diagnosis at the same anatomic site (mediastinum) and the supraclavicular lymph nodes as well. No further anthracycline was administered in two patients who received DHAP or IGEV followed by high-dose therapy and autologous stem cell transplantation (HDT-ASCT) and Radiotherapy (RT) in one. The third patient received four cycles of BEACOPP- baseline. Assuming a background crude annual rate of 3/100.000 persons for HL, 0.063 cases would have been expected over 2,093 person-years of observation of the PMLBCL cohort; the observed/expected ratio of HL cases was 47.6 (3/0.063; Poisson p=4 x10-5). The 10-year CI of HL was 1.9% (95% CI: 0.5-5.3%) using competing risk analysis:. it was 0% vs 6.0% (1.3-16.0%) respectively in patients who received RT or not after R-chemotherapy (p=0.014) and 0% vs 5.2% (1.2-14.1%) after R-CHOP (p=0.022). Although, all HLs developed after R-CHOP [10-year CI 1.9% (0.5-5.2%) vs 0% after R-DA-EPOCH], this was not statistically significant (p=0.879).

CONCLUSION: The event of sequential cHL after PMLBCL generally occurs several years after the primary diagnosis and almost always involves the mediastinum. This is the first report exclusively focused on the subject in three independent cases of a well-defined database and provides for the first time an estimation of the cumulative incidence of this event reaching 1.9% at 10-years. Interestingly, all three cases involved the mediastinum and developed in non-irradiated patients following R-CHOP and this was statistically significant. The collection of data and further work will be required in order to further elucidate the underlying biology and optimal treatment of cHL complicating PMLBCL.

P31. SUCCESSFUL SALVAGE OF PRIMARY PROGRESSIVE HODGKIN LYMPHOMA WITH THE COMBINATION OF POST-TRANSPLANT BRENTUXIMAB VEDOTIN AND RADIOTHERAPY: COMBINING NOVELTY AND TRADITION

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OBJECTIVE: Although classical Hodgkin lymphoma (cHL) is curable, 20-30% of the patients experience treatment failure. Patients who develop primary progressive disease (PD) during or very early after treatment completion generally fare worse compared to those who have residual but active disease after primary induction therapy or relapse after a complete remission (CR). High-dose therapy with autologous stem cell transplantation (ASCT) remains the standard of care. However, ASCT may not always be feasible in the above subgroup due to chemorefractoriness, so that alternative treatment strategies are urgently needed. The present report aims to describe the potential role of radiotherapy (RT) in conjunction with brentuximab vedotin (BV) consolidation after ACST in patients with primary progressive cHL, a propose of 2 cases who proved to be also refractory to second-line therapy and achieved only partial responses with third-line BV-chemotherapy combination, thus permitting ASCT.

METHODS: We describe 2 cases of nodular sclerosing cHL (NS-cHL), classified as early unfavorable (intermediate) stage IIA with cervical, supraclavicular and mediastinal lymphadenopathy, who developed PD during or within 1 month from the completion of ABVD (adriamycin, bleomycin, vinblastine, dacarbazide) regimen. After salvage chemotherapy with IGEV (ifosphamide, gemcitabine, vinorelbine, steroids), both patients experienced refractory disease (Deauville 5-point scale score 5 on PET/CT) and were forwarded to third-line BRESHAP (BV, etoposide, steroids, high-dose cytarabine, cis-platinum) achieving partial response (PR) and thus becoming eligible for ASCT.

RESULTS: Patient #1: Post-transplant PET/CT -around 45 days later- remained positive (D5 PS score 4), clearly compatible with residual active disease, and BV consolidation was started for "primary refractory disease"with multiple risk factors according to the AETHERA schedule. While receiving BV consolidation, she also underwent RT with potentially curative intent (36 Gy at the initially involved field plus 10 Gy at persistent disease). CR was demonstrated by PET/CT post-RT and the patient completed 16 cycles of BV uneventfully. She remains in CR 27 months after stem cell infusion. Patient #2: Post-transplant PET/CT -around 45 days later- revealed D5 PS score 3 (positive per Cheson 2007 but borderline per Lugano 2014 criteria) and BV consolidation was initiated for "primary refractory disease". After 4 cycles (7 including BRESHAP) BV was discontinued due to neurotoxicity. Meanwhile, the patient underwent 36 Gy RT at the sites of presumably persistent disease and post-radiation PET/CT was still interpreted as D5 PS score3. The patient remains in remission 21 months after stem cell infusion.

CONCLUSION: The present report demonstrates the feasibility of the concomitant BV consolidation and RT very soon after ASCT as a potentially curative therapeutic approach. We also propose the potential efficacy of this strategy in patients with refractory cHL with relatively localized disease prior and after ASCT. The key takeaway message is that RT should not be ignored in appropriate patients with cHL who are scheduled for early BV consolidation after ASCT. Both modalities may provide the chance for cure in selected patients, probably without important additive toxicity.

P32. BURKITT AND BURKITT-LIKE LYMPHOMA: TREATMENT OUTCOMES WITH R-HYPERCYVAD/HDMTX-CYTARABINE REGIMEN

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OBJECTIVE: Burkitt Lymphoma (BL) and Burkitt-Like Lymphoma are highly aggressive B-cell Non Hodgkin Lymphomas (NHL) that require immediate diagnostic and therapeutic intervention. There are 3 subtypes: sporadic, endemic and immunodeficiency-associated. Sporadic is observed in USA and Western Europe and is associated with Epstein-Barr virus. It often presents as abdominal masses with central nervous (CNS) and bone marrow involvement. Intensive chemotherapy regimens such as HyperCYVAD/HDMTX-Cytarabine in combination with Rituximab and CNS prophylaxis improved prognosis and survival rate significantly.
METHODS: We retrospectively studied 37 newly diagnosed patients with BL and Burkitt-Like Lymphoma that were treated in our department between 2008-2020.
RESULTS: Thirty-seven patients were evaluated, 16 females and 21 males. The median age at diagnosis was 40 y (14-83). Out of 37 patients, 9 (24%) were over the age of 60 y, while 6 (16%) were under 20 y. Seventeen patients (46%) presented with abdominal mass, 6 (16%) had CNS involvement and 8 (21%) had bone marrow involvement. The majority of patients (74%) had advanced stage disease (III and IV), as well as high serum Lactate Dehydrogenase (LDH) levels (71%), whereas 13 (39%) presented with B-symptoms. Four patients were treated with R-CHOP due to advanced age and poor performance status. The rest 33 (89%) received the R-HyperCYVAD/HDMTX-Cytarabine protocol. The median number of chemotherapy cycles administered was 7 (range 1-11), while 2 patients received complementary radiation therapy. The therapeutic regimen was highly effective: 30/33 (91%) achieved complete remission (CR) and no one relapsed. However, current treatment had significant hematologic and neurologic toxicity. All 33 patients had grade IV neutropenia, anemia and thrombocytopenia and required GCSF support and blood product transfusions. Severe neuropathy (grade ≥2) occurred in 16/33 (48%). Dose adjustments were necessary in 12 (36%) patients. Treatment had to be permanently discontinued in one patient, where two switched to an alternative regimen. The toxicities were reversible in all cases except for one: patient who developed myelitis and subsequently permanent paraplegia. Five-year overall survival (OS) was 90%. Four patients died, 3 due to refractory disease and 1 due to sepsis. Late adverse events were myelodysplastic syndrome (1) and grade IV respiratory infection in the patient with the paraplegia.
Conclusion: Although application of R-HyperCYVAD/HDMTX-Cytarabine protocol in BL and Burkitt-Like Lymphoma is effective, the toxicity is also quite high. The main problem remains the drug-associated neurotoxicity caused by vincristine, high doses of methotrexate/cytarabine and lumbar puncture infusions. Prompt identification of adverse events and early neurophysiology performance exam are crucial as may prevent permanent damage through dose adjustments.

P33. LEUKEMIC TRANSFORMATION OF A CASE OF ESSENTIAL THROMBOCYTHEMIA WITH A RARE GENETIC MUTATION

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OBJECTIVE: INTRODUCTION Essential Trobocythemia (ET) is in the BCR-ABL negative chronic myeloproliferative diseases (CMPD) group, and it has the least leukemic transformation risk among CMPDs. Although some chromosomal abnormality can be seen in leukemic transformation, no specific abnormality has been identified. Here, we present a rare case of ET who developed leukemic transformation after thrombocytosis for ten years.

METHODS:

RESULTS: CASE PRESENTATION A 67-year-old male patient applied for further examination due to high thrombocyte and leukocyte values at an external center. It was learned that the patient's thrombocyte values had been high for about 10 years, and that the leukocyte value had also increased for the last four months. However, there was no diagnosis of any hematological disease for these findings. Thirty five years ago, an enlarged inguinal lymph node excisional biopsy revealed "lymphocytic type malignant lymphoma" so he received radiotherapy without chemotherapy. He has a history of hypertension and left bundle branch block and is using valsartan + hydrochlorothiazide. In the complete blood count at first admission, hemoglobin: 11.3 g/dL (13.5-18), MCV: 105 fl (80-96), platelets: 690.000/mm3 (150.000-400.000), leukocyte: 13.750/mm3 (4500-11,000), neutrophil: 5.680/mm^3 (2.000-7.800), lymphocyte: 3.580/mm^3 (1.000-4.000), monocyte: 3.641/mm^3 (0-100), basophil: 814/mm^3, (0-200), eosinophil: 280/mm^3, (0-700) were detected. Biochemical tests revealed LDH: 247 U/L (125-220), Vitamin B12: >2.000 (197-866). Other than that, no significant abnormality was found in CRP, ESR and other biochemical tests. In the peripheral smear, a marked increase in platelet clusters, an increase in the leukocyte series, a shift to the left, and atypical lymphoid cells were observed. There were also very few myeloblast-like cells and normoblasts. In bone marrow biopsy, 23% of CD34, CD117, MPO positive blastic cells were detected. In genetic evaluations: JAK2 V617 F was negative, BCR-ABL was negative. In the bone marrow culture and chromosomal analysis: 46 XY, +10, +21 were found. In the FISH examination, three signals belonging to the 21 q22 region were detected in 90% of the cells with the t (8; 21) probe. With these findings, the patient was diagnosed with leukemic transformation of Essential Thrombocytosis. The treatment of the patient, whose blood values remained stable, was delayed for one month due to the Covid-19 pandemic. At the control one month later, Azacitidine treatment was started because the thrombocyte, leukocyte and blast count increased. Blast rate in bone marrow assessment after three cycles was 5.6% in flow cytometry and 15% in biopsy. The treatment of the patient continues.

Conclusion: DISCUSSION In the ET patient who developed leukemic transformation; Genetic abnormalities of t (8; 21), trisomy 10, trisomy 21 have not been previously reported. It is an important feature that our patient had a history of lymphoma 35 years ago. We think that transformation should be taken into consideration when evaluating CMPD patients. In addition, secondary malignancies should be kept in mind while evaluating patients.

P34. POLYMYOSITIS AS A PARANEOPLASCTIC SYNDOROME IN HODGKIN LYMPHOMA: A CASE REPORT

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OBJECTIVE: Paraneoplastic syndromes are frequently observed as an important finding of primary diseases. These disorders are caused by hormones, peptides, or cytokines or from immune cross-reactivity between malignant and normal tissues. The endocrine, neurologic, dermatologic, rheumatologic, and hematologic systems can be affected. Breast cancer, lung cancer, gynecologic tumors, and hematologic malignancies are the most common primary malignancies. Paraneoplastic neurological syndromes are rarely seen with Hodgkin lymphoma but polymositis is reported in some cases. The importance of the early detection of a paraneoplastic syndrome is to lead to the treatment of the primary tumor, which is also crucial in the management of paraneoplastic syndromes.
Methods: We here aim to report a case of hodgkin lymphoma presented with polymyositis.
RESULTS: A thirty-seven-year-old male presented with pain in right and left knees which increases with movement and weakness in bilateral extremities for the last two months. The patient had a history of severe B symptoms including 20 kilograms of weight loss. On physical examination, the patient appeared pale and dehydrated, and proximal muscle weakness was detected. In laboratory findings, erythrocyte sedimentation rate was 110 mm/h and CRP: 78 mg /L, creatine kinase (CK) was measured as 3072 mg/l. Peripheral blood tests revealed pancytopenia. Electromyography was performed to the patient whose physical examination revealed proximal muscle weakness. EMG showed large fiber polyneuropathy and myopathy. Quadriceps muscle biopsy was performed and it was reported as findings compatible with polymyositis. PET-CT imaging demonstrated widespread FDG uptake in skeletal system (SUVmax: 11.7), liver (SUVmax: 6.1), mediastinal paratracheal, paraaortic lymph nodes (SUVmax: 15.4), abdominal lymph nodes (SUVmax: 12.5), left supraclavicular lymph node (SUVmax: 14.8). Left supraclavicular lymph node excisional biopsy was performed and the result was noduler sclerosing Hodgkin lymphoma. Bone marrow biopsy showed Hodgkin lymphoma infiltration. The patient received adriamycin (25 mg/m^2/day), dacarbazin (375 mg/m^2/day), vinblastin (6 mg/m^2/day) and bleomycin (10 mg/m^2/day) every 14 days (ABVD protocol). After one cycle of ABVD protocol, the patient's symptoms of proximal muscle weakness disappeared completely, while CK levels regressed to the normal range. After 6 cycles of ABVD protocol, it was shown that a complete response was obtained in PET-CT.
CONCLUSION: Although neurological paraneoplastic syndromes are rarely encountered in the course of Hodgkin lymphoma, examination of these non-metastatic systemic findings for a possible primary malignancy will play an important role in the detection and treatment of the disease.

P35. THE CONTRIBUTION OF AZACITIDINE AND DECITABINE MAINTENANCE TO TREATMENT IN NEWLY DIAGNOED ELDERLY AML PATIENTS: REAL LIFE DATA

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OBJECTIVE: Our aim is to answer the question of whether azacitidine and decitabine which are being used in first line therapy should be used until progression with real-life data in patients with advanced age and fragile acute myeloid leukemia (AML), who are not generally included in clinical trials.
METHODS: Comparing overall survey of the two centers that planned treatment with HMAs until progression and planned 6 cures of treatment independent of the response due to side effects in the fragile group.
RESULTS: The study included 41 AML patients with a median age of 75 years and a performance score of 3 and 4 among 56%. Among them, 20 were planned to give maintenance until progression and 21 were planned to take 6 cycles. In the study, a median survey of 7.5 and 3 months was obtained in the maintenance positive and negative groups, respectively ($p < 0.05$).
Conclusion: Exposure to long-term HMA therapy appears to be a risk for adverse effects in elderly and fragile AML patients, but treatment until progression is significantly superior in terms of overall survey.

P36. INDOLENT HODGKIN LYMPHOMA WITH NASOPHARYNGEAL INVOLVEMENT: A CASE REPORT

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OBJECTIVE: Lymphomas are the third most common malignancy of the head-neck area after squamous cell carcinoma and thyroid cancers with a frequency of 12%. Hodgkin's lymphomas also account for 4% of this group. The incidence of nasopharyngeal involvement in patients diagnosed with HL in studies is less than 1%.
METHODS: We here aim to report an indolent Hodgkin lymphoma patient with nasopharyngeal involvement.
RESULTS: 34-year-old female, no comorbid disease except hypothyroidism. Upon the detection of a 33 mm lesion in the inferior part of the nasopharynx with a thickness of 8 mm in the neck mri imaging performed under polyclinic control in the patient who applied to orthopedic outpatient clinic with complaints of neck pain, histopathological diagnosis has been requested from the patient and pet ct has been recommended for staging purposes. Mass excision has been performed from the patient. As a result of pathology, staining with cd 15, cd 30 pax5, poor staining with oct2 in a small number of reed-stenberg-like cells have been observed and evaluated in favor of lymphocyte-rich type Hodgkin's lymphoma and reported in this way. Thereupon, the patient has undergone a pet ct. No additional focus has been detected in the pet ct. Based on the available data, the patient has been decided to apply ABVD (Adriamycin (doxorubicin) 25 mg/m^2, Bleomisin 10 mg/m^2, Vinblastin 6 mg/m^2 or Dacarbazine 375 mg/m^2, IV) protocol. After 2 cycles of abvd chemotherapy imaging revealed a decrease in mass size, it has been planned to complete the treatment with 6 spheres. It has been observed that the mass completely disappeared in the post-treatment response evaluation of the patient who completed 6 courses of chemotherapy without any problems.
CONCLUSION: Although nasopharyngeal involvement in Hodgkin's lymphoma is rare, it should always be remembered among head and neck cancers.

P37. SECOND LINE THERAPY IS A STRONGER PROGNOSTIC FACTOR FOR OVERALL SURVIVAL COMPARED WITH FIRST LINE THERAPY IN MULTIPLE MYELOMA: REAL-WORLD DATA FROM A SINGLE CENTER

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OBJECTIVE: Novel therapies have improved response and survival rates in Multiple Myeloma (MM). Outside clinical trials, the prognostic significance of the type of second line therapy in overall survival (OS) has not been widely investigated. Our aim was to explore the efficacy and the prognostic impact of 2 nd line therapy in comparison with 1 st line treatment and other important prognostic factors for OS.
Methods: We studied 300 MM patients (M/F: 154/146, median age: 67, range: 38-88, IgG: 160. IgA: 88, light chain: 38, non-secretory: 13, IgD: 1), who received 2 nd line therapy and were followed for a long period of time; 128 received lenalidomide-dexamethasone (Ld) (group1: n=82) or Len-based triplets (LBT) (group2: n=46), such as ixazomib-Ld (n=17), carfilzomib-Ld (n=14) or daratumumab-Ld (n=15). Group 3 (n=172) was treated with thalidomide-based regimens (n=62), bortezomib-based regimens (n=68) or conventional therapy (n=42). All groups were compared according to age, International Staging System (ISS) and revised ISS (RISS), estimated glomerular filtration Rate (eGFR-CKD-EPI), β2 microglobulin (β2 M), lactate dehydrogenase (LDH), type of induction therapy and response rates ((Pearson's x2 test, Mann-Whitney-U test και One-Way ANOVA). Prognostic parameters for OS were evaluated with cox regression. Progression free survival (PFS) after 2 nd line therapy and OS were plotted with Kaplan-Meier; p <0.05 was considered as statistically significant.
Results:: At baseline patients in group 3 had more frequent advanced stage (ISS3/RISS3) and abnormal LDH; There was no difference between groups for age, β2 M and eGFR. Induction with novel agent-based therapies was distributed as follows: group 1: 78%, group 2: 98%, group 3: 43% (p <0.001). Response rates after induction therapy did not differ between groups (p >0.05). After second line therapy, patients of group 2 displayed higher complete response (CR) rate (p <0.001). After median follow-up from 2 nd line therapy 6,8 years (95% CI: 5,5-8,1) PFS for groups 1, 2, and 3 was 14, 17 and 11 months respectively (p=0.04). Univariate analysis showed that RISS, eGFR, peripheral stem-cell transplantation (PBSCT) and type of 2 nd line therapy were independent prognostic factors for OS. 1 st line therapy, LDH and β2 Mdid not display prognostic significance. In the multivariate analysis, type of 2nd line therapy, RISS and eGFR maintained strong prognostic significance for OS. After a median follow up of 10 years (95% CI: 7-12), median OS for group 1 and 3 was 68 and 43 months, respectively, whereas for group 2 the median OS has not been reached (p <0.001); 3-year OS after initiation of 2nd line therapy for group 1, 2, and 3 was 41%, 71% and 31% respectively (p=0.001).
CONCLUSION: Len-based triplets confirmed superiority regarding quality of response over other 2nd line therapies in the real-world setting. Type of therapy administered in 2 nd line proved to be a stronger prognostic factor for OS compared with induction therapy, underlying the importance of offering "curative" therapies beyond 1 st line.

P38. EFFICACY OF DARATUMUMAB MONOTHERAPY ON BONE METABOLISM OF PATIENTS WITH ADVANCED RELAPSED/REFRACTORY MULTIPLE MYELOMA: RESULTS FROM THE PHASE 2 REBUILD STUDY

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OBJECTIVE: Osteolytic lesions (OL) is a devastating characteristic of multiple myeloma (MM) that decreases patients (pts) quality of life. The aim of the REBUILD study is to evaluate the effect of dara monotherapy on bone metabolism in advanced relapsed/refractory multiple myeloma (RRMM) pts.
METHODS: REBUILD is a prospective, open-label, multicenter, phase 2 study which has completed the enrollment of 57 pts with documented RRMM and ≥2 prior lines of therapy, including lenalidomide and a proteasome inhibitor. Pts receive dara at a weekly dose of 16 mg/kg for Cycles 1-2, every 2 weeks for Cycles 3-6 and every 4 weeks thereafter. The primary endpoint of this study was the change from baseline in the bone resorption markers C-terminal telopeptide of collagen type I (CTX) and tartrate-resistant acid phosphatase isoform 5 b (TRACP-5 b) after 4 months of dara monotherapy. Secondary endpoints include the change at 4 months from baseline in bone formation markers (bALP, OC and PINP); markers of osteoclast regulation (RANKL, OPG and CCL-3); markers of osteoblast control (sclerostin, dickkopf-1 [DKK-1]), and PFS.
RESULTS: Fifty-seven pts were enrolled in 6 sites; among them 29 pts had bone markers and clinical data available on baseline and after 4 months of study treatment and are included in the present analysis. Median age was 73 years, and approximately half of them were female (15 pts, 52%). Median number of previous therapies was 3 (range: 2-5). Fifteen pts (52%) had >10 osteolytic lesions at study initiation, and only 4 pts (14%) received bisphosphonates together with dara monotherapy. The median changes in CTX and TRACP-5 b levels for all pts (n=29) after 4 months in study treatment were 3.9% and -2.2%, respectively. Overall, 10 pts (35%) had ≥ 30% reduction in CTX and 5 pts (17%) in TRACP-5 b levels. The median changes in bone formation markers for all pts after 4 months of dara were 24.5% for bALP, 116.8% for OC, and 15.7% for PINP. The differences for pts with a response versus pts without a response were respectively 26% versus 18% for bALP, 190% versus -61% (p=0.020) for OC, and 22% versus -3% for PINP. Other major differences in 4 months of dara monotherapy were the decrease in DKK-1 by 49% in pts with a response versus 2% increase in pts with no response, and the decrease in CCL3 by 15% in pts with response versus 101% increase in pts with no response (p=0.039). The median PFS for all 51 pts was 4.6 months (95% CI: 2.8-7.2).
Conclusion: Monotherapy with dara has a positive effect on bone metabolism even in these highly pre-treated pts with MM. Reduction of TRACP-5 b and of CCL-3 in responsive pts suggests an inhibitory effect on osteoclasts by dara. Interestingly, we found that there is a strong bone formation effect in all pts treated with dara monotherapy, especially in those who responded to therapy, i. e. OC had a 2-fold increase after 4 months of therapy. This is at least partially due to the reduction of DKK-1 (osteoblast inhibitor) in responding patients.

P39. EFFICACY AND TOLERABILITY OF DARATUMUMAB WITH IXAZOMIB AND DEXAMETHASONE IN PATIENTS WITH ONE PRIOR LENALIDOMIDE-BASED REGIMEN: PRELIMINARY RESULTS OF THE PHASE 2 DARIA STUDY

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OBJECTIVE: Second-line treatment of patients who are refractory to lenalidomide or have relapsed after prior use of lenalidomide is challenging. The aim of the DARIA study is to evaluate the effectiveness of daratumumab in combination with ixazomib and dexamethasone (Dara-Id) as second-line therapy in patients who have received prior treatment with lenalidomide-based regimens.
METHODS: DARIA is an ongoing prospective, open-label, multicenter, phase 2 study, which aims to enroll 43 patients who have received one prior line of therapy with a lenalidomide-based regimen. The treatment phase consists of an induction therapy for 9 cycles, followed by a maintenance period. The induction phase included 28-day treatment cycles with 16 mg/kg intravenous daratumumab (weekly for cycles 1-2, every 2 weeks for cycles 3-6, and every 4 weeks thereafter), 4 mg oral ixazomib (Days 1, 8, and 15 of each cycle), and 40 mg oral dexamethasone for the first 9 cycles (weekly, each cycle). During the maintenance phase of the study daratumumab is administered every 4 weeks and ixazomib on the same schedule, until disease progression or unacceptable toxicity whereas dexamethasone is discontinued. The primary endpoint is the overall response rate (ORR). Secondary endpoints include evaluation of the toxicity profile of the study treatment, PFS, overall survival, and levels of serum bone markers and angiogenic cytokines.
RESULTS: Fifteen patients, enrolled in 4 sites, are included in the current analysis. Overall, 60% of the patients were refractory to lenalidomide. Median age was 70 years and the majority of patients were male (60%). The median time from diagnosis to first dose of study treatment was 1.3 years. Two patients (13%) had a prior autologous stem cell transplantation. At screening 47%, 26%, and 27% of the patients had an international staging system (ISS) of 1, 2, and 3, respectively, and a revised ISS of 1 (21%), 2 (71%), and 3 (7%). The median number of cycles reached until the cut-off date was 7. The median time from first dose of study treatment until first partial (PR) or very good partial response (VGPR) was 0.9 month. ORR was 60%, with 47% of the patients achieving VGPR and 13% PR. The 12-month PFS rate was 54%, and 8 patients (53%) were still on treatment by the cut-off date. From the patients who discontinued 71% was due to disease progression and 29% due to physician's decision. Overall, 10 patients (67%) had at least one adverse event (AE) grade 3 or 4, the most common being thrombocytopenia (6 patients, 40%). Four patients (27%) had a single SAE each: lower respiratory tract infection (fatal); peritonitis, gastroenteritis; nephrolithiasis.
CONCLUSION: Rapid and deep responses were observed following treatment with daratumumab, ixazomib and dexamethasone as second-line therapy in patients who were previously treated with a lenalidomide-based regimen, more than half of whom were refractory to lenalidomide. The safety profile of Dara-Id combination is very good with one third of the patients not experiencing any grade 3 or 4 AEs, when at the same time the PFS rate at 12 months reached 54%.

P40. DARATUMUMAB WITH DEXAMETHASONE IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA AND SEVERE RENAL IMPAIRMENT: RESULTS ON EFFICACY AND SAFETY OF THE PHASE 2 DARE STUDY

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OBJECTIVE: Renal impairment (RI) is common in multiple myeloma (MM), with up to 40% of the patients (pts) experiencing this complication during the course of their disease. DARE is a prospective, open-label, multicenter, phase 2 study, which completed the enrollment of 38 adult pts with documented RRMM and severe RI, defined as either eGFR<30 mL/min/1.73 m2 or requiring hemodialysis.
Methods: Pts receive 28-day treatment cycles with 16 mg/kg intravenous daratumumab (weekly for cycles 1-2, every 2 weeks for cycles 3-6, and every 4 weeks thereafter) and oral dexamethasone (40 mg weekly, each cycle). The primary endpoint is progression-free survival (PFS). Secondary endpoints are overall response rate (ORR; proportion of pts with partial response or better), renal response rate as evaluated per IMWG criteria (RRR; proportion of pts with best response of renal partial response or better), and safety. All responses are based on investigators' assessment per International Myeloma Working Group criteria. This preliminary analysis presents results for pts who received the first dose of study treatment at least 5 months prior to the cut-off date (01/05/2020).
RESULTS: The current analysis includes 35 pts, enrolled in 7 Sites. Median age was 72 years, and 77.1% were male. The median time from diagnosis to first daratumumab dose was 4.2 years. Pts had a median of 3 prior systemic therapies, and 37.1% had a prior autologous stem cell transplantation. At study initiation 8.6% and 91.4% of pts had international staging system (ISS) 2 and 3 disease, respectively, while 51.4% and 48.6% were revised ISS 2 and 3. The median eGFR at baseline was 13 mL/min/1.73 m2. and 17 pts (48.6%) were on dialysis. The median number of cycles administered until the cut-off date was 5 and the median follow-up duration was 5.5 months. The 6-month progression-free survival rate, was 50% (figure). Overall, ORR was 45.7%, with 31.4% of all pts achieving a VGPR and 14.3% a PR. For pts on dialysis (n=17), ORR was 35.3%, equally divided between pts achieving VGPR and PR (17.6%). The median time from the first dose of study treatment until the first response (≥PR) was 0.9 months. RRR was 17.1%. By the cut-off date, 37.1% of the pts were still receiving protocol therapy, 17.1% discontinued treatment due to death, and 31.4% due to disease progression. Overall, 17 pts (48.6%) had at least 1 adverse event (AE) of grade 3 or 4, most frequent being anemia (17.1%) and hyperglycemia (8.6%). Nine (25.7%) pts had at least 1

SAE: Septic shock (fatal, 2 pts), and performance status decreased (fatal), lower respiratory tract infection (fatal), myocardial infarction (fatal), peritonitis (fatal, in a patient receiving peritoneal dialysis), cerebrovascular accident, pneumonia, acute kidney injury, and hyperkalemia (1 pt each). **Conclusion:** The administration of daratumumab with dexamethasone led to rapid hematologic responses in pts with RRMM and severe RI, including those in dialysis, and at the same time it resulted in a major renal response for 17.1% of the pts. Importantly, new safety signals were not observed, and daratumumab can be safely administered in pts with severe RI or those on dialysis.

P41. SOLUBLE UROKINASE-TYPE PLASMINOGEN ACTIVATOR RECEPTOR (SUPAR) AS A BIOMARKER OF RENAL OUTCOMES IN AL AMYLOIDOSIS

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OBJECTIVE: Soluble Urokinase-Type Plasminogen Activator Receptor (suPAR) is the circulating form of a glycosyl-phosphatidylinositol-anchored three-domain membrane protein. suPAR is expressed on a variety of cells, including immunologically active cells, endothelial cells, and renal podocytes. The aim of the study was to evaluate suPAR, as a potential new biomarker for renal outcomes in patients with AL amyloidosis treated with contemporary therapies.
METHODS: We measured serum suPAR levels in 136 patients with AL amyloidosis, before start of therapy and at 6 months in 98 of them. Serum suPAR levels were determined using a standard commercial enzyme-linked immunosorbent assay (suPARnostic Standard kit; ViroGates A/S, Birkerød, Denmark).
Results: The median age was 65, 56% were males, 72% had renal, 71% heart, and 17% liver involvement; Mayo stage disposition was 15%, 56% and 29% and renal stage disposition 39%, 44% and 17%, respectively; 82% received bortezomib-based therapy. Median baseline suPAR levels were 6.6 ng/mL (range 2.7-29.0 ng/mL), which is significantly higher than in other studies in non-amyloidosis patients with CKD or CAD/CHF (median 3.04-3.7 ng/ml). We observed a weak negative correlation of suPAR levels with eGFR, but there was no correlation with proteinuria or serum albumin levels in patients with AL amyloidosis and was not associated with renal stage (as defined by eGFR<50 ml/min and proteinuria >5 gr/d). suPAR levels were higher in patients with heart involvement and were associated with NT-proBNP (p=0.003), hs-TnT (p<0.001) and Mayo stage. suPAR levels were higher among those with liver involvement and strongly correlated with alkaline phosphatase levels (p<0.001). There was also a positive correlation with involved Free Light Chain (iFLC). At 6 months suPAR levels were 6.1 ng/mL and in pairwise comparison this reduction was marginally significant (p=0.039); however, this reduction was independent of baseline level and of hematologic response. Baseline suPAR levels were associated with higher probability of eGFR decline (p=0.008) and with renal progression per consensus criteria (p=0.02), at 6 months. Furthermore, suPAR levels at 6 months were strongly associated with the probability of progression to dialysis (2% vs 20% at 2 years and 2% vs 38% at 4 years, p<0.001), independently of renal stage, of renal progression by standard criteria at 6 months, and of the depth of hematologic response (no response vs PR vs VGPR/CR). A reduction of suPAR levels at 6 months compared to baseline was also associated with lower probability of progression to ESRD requiring dialysis, independently of baseline eGFR, baseline renal stage and hematologic response.
CONCLUSION: In patients with AL amyloidosis suPAR levels are prognostic of renal outcomes, especially with progression to ESRD requiring dialysis. Most importantly, suPAR levels and their changes were independently associated with renal progression and progression to dialysis either when measured before start of therapy or at 6 months, independent of baseline renal stage, renal progression by the Palladini criteria and even of the quality of hematologic response. Further evaluation in larger cohorts is required to evaluate suPAR as a biomarker for renal outcomes in AL amyloidosis.

P42. PERIPHERAL BLOOD IMMUNE PROFILING OF MULTIPLE MYELOMA PATIENTS AT DIAGNOSIS; CORRELATIONS WITH CIRCULATING PLASMA CELLS

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OBJECTIVE: Circulating Tumor Plasma Cells (CTPCs) detected in the peripheral blood (PB) of newly diagnosed Multiple Myeloma (MM) patients have been associated with adverse prognostic features and poor overall survival. The correlation of CTPCs with the immune profile in PB remains unknown. The aim of the present study was to evaluate the immune profile in the PB of patients with newly diagnosed MM and correlate the results with the presence of low or high number of CTPCs.
METHODS: We analyzed myeloid-derived suppressor cells (MDSCs) and major immune T cell subpopulations, including regulatory T cells (Tregs), in the PB of newly diagnosed MM patients. The percentages of MDCSs and Tregs were correlated with the concomitant presence of low (<0.003%) or high (>0.05%) CTPCs. PB samples of 26 newly diagnosed MM patients were analyzed with flow cytometry using the following panels: a) the minimal residual disease EuroFlow-based next-generation flow cytometry (NGF) panel, for the detection and identification of PB CTPCs; b) a panel comprising the surface markers CD15, HLA-DR, CD14, CD124, CD33, CD11 b, and LinCD56-CD3-CD19, for the detection of polymorphonuclear MDSCs (PMN-MDSCs), monocytic MDSCs (M-MDSCs) and early-stage MDSCs (eMDSCs); and c) two panels comprising the surface and intra-cellular markers CD25, CD3, CD39, CTLA-4, CD4, CD8, CD45 RO, CD45 RA, HLA-DR, CD127, Ki67, and FoxP3, for the detection of CD4, CD8 T cells and Tregs. For the evaluation of b) and c), prior to staining, mononuclear cells (PBMCs) were isolated from PB using density-gradient centrifugation on Ficoll-paque.
Results: Using NGF, 12 MM patients had high and 14 low CTPCs in their PB. MDSCs averaged 5.42 ± 5.9% of PBMCs, whereas PMN-MDSCs were the most abundant subpopulation (4.38 ± 5.7% of PBMCs) and displayed great heterogeneity between patients. Additionally, 22 distinct T subpopulations were phenotypically identified and analyzed, including CD4 and CD8 T cells, naive Tregs (CD45 RA+), effector Tregs (CD45 RO+), terminal effectors (HLADR+), CD39+ suppressor Tregs, CD8 Tregs and their proliferating (Ki67+) counterparts. Comparing the percentages of the immune populations among patients with high versus low CTPCs, M-MDSCs were significantly more abundant ($p<0.05$) in patients with low CTPCs, whereas immune profiling of T cells revealed (although not reaching statistical significance) the presence of increased percentages of proliferating Tregs in those with low CTPCs and increased percentages of naïve CD4 T cells in patients with high CTPCs.
CONCLUSION: To our knowledge, this is the first study correlating the presence of high versus low CTPCs with the immune profile in PB of MM patients. Low CTPCs correlated with the presence of higher percentage of M-MDSCs. Since the latter has been associated with the CCR5-dependent recruitment of Tregs into the tumor site, our findings suggest that, in low CTPC MM patients, a more effective immune surveillance mechanism, mediated by the interaction of M-MDSCs - Tregs, likely controls CTPC expansion and may contribute to a more favorable prognosis. Analysis of more samples, which is ongoing, will validate our findings and provide more solid results.

P43. THROMBOTIC AND BLEEDING COMPLICATIONS IN PATIENTS WITH AL AMYLOIDOSIS

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OBJECTIVE: Thromboembolic complications are common in patients with plasma cell dyscrasias. In AL amyloidosis, however, both a risk of thromboembolism and of bleeding co-exist, but the relevant risks have not been thoroughly evaluated. In the current analysis we aimed to describe thrombotic and embolic events as well as bleeding complications in a series of AL patients treated and diagnosed in the recent era.
METHODS: We analyzed the records of 300 patients with AL amyloidosis who were followed and treated in a single center to identify clinically relevant episodes of venous and arterial thromboembolic events and of bleeding events.
RESULTS: 56% of the patients were males, median age was 65 years; 113 (38%) patients received antiplatelet therapy, 49 (16%) antithrombotic prophylaxis with LMWH, 34 (11%) prophylaxis with acenocoumarol, and 9 (3%) with NOACs. The median follow-up of the cohort is 55 months. After the diagnosis of AL amyloidosis, 20 (6.7%) patients developed at least one venous thrombosis event (VTE) (DVT: 3%, Pulmonary embolism: 2.3%, other: 1.4%). In 20 (6.7%) patients an arterial event (AEE) (stroke: 3.3%, AMI: 2.4%, other: 1%) was recorded; however, another 24 (8%) patients had a history of AEE prior to diagnosis of the disease and in 5 (1.7%) patients this occurred within 1 year from the diagnosis of AL amyloidosis. Median time from diagnosis to the first VTE was 31 months and to the first AEE was 14 months. In 13/20 patients with VTE and in 10/20 with AEEs the events occurred while on anti-plasma cell therapy. On the other side, we identified 36 (11%) patients with at least one clinically significant bleeding event (GI: 5.3%, CNS: 1.7%, Other: 4%) which was the cause of death in 7/36 patients. Risk factors for VTEs included renal involvement (p=0.047), lower albumin levels (p=0.022), lower eGFR, more extensive bone marrow infiltration (0.012), soft tissue involvement (p=0.029) and a history of prior thrombosis (p=0.001); use of IMiDs was associated with high risk (p=0.001). AEEs were more common in men (p=0.043), those with renal involvement (p=0.054), but less common in those with liver involvement (0.031); a history of prior AEE was associated with a high risk of subsequent AEE (p <0.001). We found no significant associations of VTEs or AEEs with heart involvement or Mayo stage. A VTE occurred in 2.6% of patients receiving antiplatelets vs 3% of those who did not; 7% of those on antithrombotic therapy developed VTE (except one, all were in prophylactic dose of LMWH). In multivariate analysis renal involvement, lower eGFR and use of IMiDs was associated with higher VTE probability. Bleeding risk was higher in patients with liver involvement (p=0.027). Among patients receiving antiplatelets (excluding those on antithrombotic therapy) bleeding occurred in 15% (vs 13% of those not receiving) while among patients receiving antithrombotic therapy (LMWH, coumadin, NOACs) bleeding occurred in 8%.
CONCLUSION: In patients with AL amyloidosis the risk of thrombotic and arterial embolic events is significant despite the frequent use of antiplatelets and anticoagulation; however, the risk of bleeding is also high.

P44. IBRUTINIB IS A SINGLE AGENT IN CHRONIC LYMPHOCYTIC LEUKEMIA: A SINGLE CENTER EXPERIENCE

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OBJECTIVE: Bruton's Tyrosine Kinase (BTK) is one of the tyrosine kinases that play a role on the development of the B-cell malignancies. Ibrutinib, is an approved oral, once-daily BTK inhibitor and as a single agent has led to prolonged progression-free survival and overall survival in patients with previously treated chronic lymphocytic leukemia (CLL) and in treatment-naive group. The studies still continue in combination with various agents. Herein, we present the effect and side effects of single agent ibrutinib in patients both treatment-naive and relapsed-refractory patients.
METHODS: 21 patients were evaluated who were diagnosed as CLL. Age, gender, follow-up period, RAİ stage, cell blood count, peripheral smear, biochemical parameters, bone marrow aspiration and biopsy, cytogenetic results, follow-up period, treatments prior to ibrutinib, the response to the treatment and side effects were recorded, retrospectively. Response to the treatment were decided by physical examination, laboratory results or computer tomography.
RESULTS: A total of 21 patients were screened from the records. While 20 of the patients were relapsed/refractory CLL, only 1 patients was treatment naive. Median age was 66 (range 40-81) and median age at the time of diagnosis was 56 (range 33-73). 14 patients were male, and 7 were female. Median follow-up period in our study was 97 months (range 17-174). The duration between diagnosis and ibrutinib treatment was 80 months (range 4-142). Ibrutinib was administered to the patients 420 mg/per day as a standard dosage. One patient who was treated with ibrutinib as a first-line treatment, had 17 p mutation by FISH and the duration time was 4 months. He is treated 12 months with ibrutinib and still followed-up in partial remission. Before ibrutinib treatment 17 patients had stable/progressive disease and 3 patients were in partial remission. 4 patients were positive for 17 p deletion. Ibrutinib was given to the patients median 9 months (range 2-30), and the median of prior treatment before ibrutinib was 2(0-6). 3 patients had a medical history of allogeneic stem cell transplantation before ibrutinib treatment. 12 patients is still followed up with ibrutinib. Median ibrutinib period for these patients are 12 months (range 3-30). 7 of 21 patients died under the treatment or after the treatment. The most common reason of death was infections. During the treatment, one patient was diagnosed as herpes zoster. Bacterial pneumonia, fungal sinusitis, neutropenic fever, subcutaneous abscess was also observed in patients during the treatment. Non of the patients had bleeding as an adverse effect.
CONCLUSION: Ibrutinib is widely in use for CLL with acceptable progression-free survival and overall survival and effective on both treatment naive and relapsed/refractory CLL. As a result, ibrutinib can be considered as well-tolerated agents in patients and patients should be followed up closely for infections and other side effects.

P45. PREDICTORS OF OUTCOME AND THE EFFECT OF AZACITIDINE (AZA) IN INTERMEDIATE-RISK (INT-RISK) MYELODYSPLASTIC SYNDROMES (MDS): A NESTED COHORT STUDY OF THE HELLENIC NATIONAL REGISTRY OF MYELODYSPLASTIC AND HYPOPLASTIC SYNDROMES (HNRMHS).

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OBJECTIVE: The revised International Prognostic Scoring System (IPSS-R) improved our ability to predict outcomes in patients with MDS. Its major limitation, however, is the large heterogeneity within the int-risk category (~20% of all patients). Recent evidence indicates variable outcomes of int-risk patients and need for additional prognostic factors to refine prognosis. Questions about benefits of AZA in int-risk IPSS-R also remain, as the original IPSS is still used for AZA approval by most health authorities. We aimed to identify features that would help to refine prognosis in int-risk MDS and examine the effects of AZA on overall survival (OS) and leukemia-free survival (LFS).
METHODS: We performed an analysis of patients with IPSS-R 3.5-4.5 registered in the HNRMHS between 1985-2016 (data cutoff; July 7, 2016). We collected clinical, treatment, and laboratory data. Cox proportional hazard models were used for survival analysis.
RESULTS: A total of 468 patients (326 men/142 women) with int-risk IPSS-R were identified. Median follow-up was 51 months (41.6-60.4) during which 220 (47.0%) patients died. 150 patients (38.6%) developed acute myeloid leukemia (AML). Median OS and LFS were 33 (95% CI: 26.6-35.4) and 26 months (21.5-30.5), respectively. The cumulative probability of progression to AML was 21.3% at 1 year, 29.8% at 2 years, and 34.2% at 3 years; median time-to-AML-progres-

sion was 10 months (7.2-12.8). Separate analysis for IPSS-R 3.5 (n=153) and 4.0/4.5 (n=315) revealed significant between-group differences in OS (p=0.039). The overall actuarial probability of survival for patients with IPSS-R score 3.5 was 46.9% at 2 years and 31.3% at 3 years; the corresponding values for IPSS-R 4.0/4.5 were 43.0% and 25.2%. On multivariate analysis, significant risk factors for inferior OS included age >70 years, circulating blasts (≥1%), IPSS-R 4.0/4.5, and log2 Endothelial Activation and Stress Index (EASIX) >0.179 (EASIX is a recently introduced biomarker in MDS). Moreover, age >70 years (HR 1.66, 95% CI 1.25-2.21; p<0.001) and circulating blasts (hazard ratio [HR] 1.51, 95% CI 1.10-2.08; p=0.011) were the only independent predictors of shorter time-to-AML transformation. 166 patients (35.5%) received AZA. AZA-treated patients were more likely to have transfusion-dependent anemia (p=0.035) and excess marrow blasts (p<0.001) than non-AZA-treated patients. 23.1% of AZA-treated patients responded to treatment (13.7% complete remission [CR]; 9.4% partial remission). The response rate to AZA did not correlate with age, sex, performance status, IPSS, cytogenetics, white-cell count, platelets, log2 (EASIX), eGFR, LDH, peripheral or bone-marrow blast cells. The median OS of AZA-treated patients was similar to patients who did not receive AZA (32.4 vs. 30 months; p=0.368). Also, AZA did not seem to mitigate risk of AML transformation (p=0.268). However, patients in CR had significantly better OS than patients with <CR (40.9 vs. 29.4 months; p=0.005) and LFS (55.3 vs. 28 months; p=0.001).
CONCLUSION: We saw evidence of better outcomes in patients with IPSS-R 3.5 as compared with 4.0/4.5. Our results indicate that log2 (EASIX), age, and circulating blasts were associated with diminished OS and, therefore, added prognostic information to the IsPSS-R. Furthermore, AZA conferred no obvious survival advantage, excluding rare patients achieving CR (13.7%).

P46. COMMON CARDIOVASCULAR BIOMARKERS ARE INDEPENDENT PREDICTOR OF OUTCOME IN PATIENTS WITH MYELODYSPLASTIC SYNDROMES (MDS)

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OBJECTIVE: MDS comprise a heterogeneous group of clonal myeloid disorders characterized by ineffective hematopoiesis and risk of leukemic transformation. The most common cause of non-MDS-related mortality is cardiovascular disease (CVD). Lower-risk MDS patients have a two-fold higher standardized mortality ratio for CVD death, and experimental evidence suggests a relationship between accelerated atherosclerosis and clonal hematopoiesis of indeterminate potential (CHIP), a pre-MDS condition. Studies in solid tumors have shown that CVD biomarkers were strong predictors of all-cause mortality. Several prognostic systems have been developed in MDS. However, assessment of prognosis remains problematic, and no current model utilizes CVD biomarkers.

METHODS: We measured serum concentrations of high-sensitivity troponin T (hsTnT), N-terminal pro-B-type natriuretic peptide (NT-proBNP), growth/differentiation factor 15 (GDF-15), and high-sensitivity C-reactive protein (hsCRP) in 66 patients with MDS. 21,2% of these patients were categorized as higher risk (intermediate 2/high) according to the original international prognostic scoring system (IPSS). According to the revised IPSS (IPSS-R), 33.3% of our patients were intermediate risk. To track the interactions between the above biomarkers and avoid the shortcomings of an overly skewed distribution, we also calculated the geometric mean of combinations of these biomarkers. Our primary objectives were overall survival (OS) (defined the time from sampling to last follow up or death from any cause) and leukemia-free survival (LFS) (defined as the time from sampling to leukemic progression or death). Cox proportional hazard models and Kaplan-Meier estimates were used for survival analysis.

RESULTS: With a median follow-up of 8.6 months (95% CI: 7.8-9.4), the median OS and LFS for the whole cohort were 11.3 (95% CI: 9.5-13.2) and 11.1 (95% CI: 9.2-12.9) months, respectively. Univariate analysis revealed that OS and LFS were significantly influenced by IPSS, IPSS-R, cytogenetic findings (according to IPSS and IPSS-R cytogenetic risk groups), erythrocyte transfusion dependency, MDS-specific comorbidity index (MDS-CI), the median absolute values of NT-proBNP, GDF-15 and hsCRP and the median logarithmic (log2) values of hsTnT, GDF-15 and hsCRP. Of note, risk factors for CVD and pre-existing CVD did not affect OS and LFS, indicating that the correlation of survival with MDS-CI and CVD biomarkers is rather linked to non-CVD-related death. In the multivariate analysis for OS, only transfusion dependency (HR: 4.29 [95% CI: 1.76-10.4]; p=0.001), IPSS-R score ≥3.5 (HR: 9.90 [2.37-41.7]; p=0.002), MDS-CI (HR: 2.29 [1.14-4.61]; p=0.021), and the geometric mean of the hsTnT, NT-proBNP and GDF-15 values on the log2 scale (HR: 3.83 [1.84-7.94]; p<0.001) correlated independently with OS. The same parameters also held independent significance for LFS.

CONCLUSION: In this small but representative cohort of patients with MDS, we showed that a composite marker derived from a weighted combination of three CVD biomarkers (hsTnT, NT-proBNP and GDF-15) can independently predict OS and LFS. Importantly, the predictive power of the CVD biomarkers does not appear to correlate with CVD-related mortality, indicating a potential causal association between CVD biomarkers and MDS pathobiology.

P47. COMPARISON OF CHARACTERISTICS AND OVERALL SURVIVAL RATES OF MULTIPLE MYELOMA PATIENTS INELIGIBLE FOR TRANSPLANT WHO ACHIEVED SUSTAINED PARTIAL RESPONSE VS. THOSE WHO EXHIBITED COMPLETE REMISSION AFTER INDUCTION THERAPY: SINGLE CENTER REAL-WORLD DATA.

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OBJECTIVE: Complete remission (CR) is an important prognostic factor for overall survival (OS) in Multiple myeloma (MM). The prognostic significance of sustained partial response (sPR) defined as PR >24 months however, may be a sufficient goal in elderly MM patients ineligible for transplant (NTE); the characteristics and the prognostic role of sPR in NTE patients has not been sufficiently explored. Herein, we investigated the characteristics prognostic impact and OS rates of sPR in NTE patients compared with those who achieve CR after induction therapy.

METHODS: We studied 255 NTE MM patients (M/F: 130/125, median age: 68, range: 43-83, IgG: 151. IgA: 64, light chain: 31, non-secretory: 9); 62 fulfilled the criteria of sPR whereas the rest (n=193) achieved CR after induction treatment; importantly, patients in CR were considered as eligible for analysis if OS exceeded 24 months. The 2 groups were compared for standard prognostic factors such as age, International Staging System (ISS) and revised ISS (RISS), β2 microglobulin (β2 M), lactate dehydrogenase (LDH), hemoglobin (Hb), estimated glomerular filtration rate (eGFR) with Pearson's x2 test, Mann-Whitney-U test and One-Way ANOVA. Prognostic factors for the type of response (sPR vs. CR) were evaluated with binary logistic regression analysis; OS was plotted with Kaplan-Meier; $p<0.05$ was considered as statistically significant boundary.

RESULTS: Patients with sPR were more frequently >65 years, they had better performance status, higher eGFR and less often anemia, abnormal LDH, and advanced stage (ISS3/RISS3) ($p<0.05$). t (4; 14) was not detected in patients with sPR vs. 10% in the CR group, whereas del17 p was found in 2% of patients with sPR vs. 14% in the CR group; the rate of t (14; 16) or 1 q+ did not differ between groups ($p>0.05$); 71% of patients with sPR was treated upfront with novel agents compared with 24% of those in the CR group ($p<0.05$). Overall, 65% of the studied population received 2 nd line therapy (sPR vs. CR group: 51% vs. 69%; $p<0.05$). Age >65, RISS1/2 and absence of anemia (Hb<10 g/dL) were independent predictors for the type of response (sPR vs. CR) ($p<0.05$). In the univariate analysis, established markers such as ISS, RISS and LDH confirmed their prognostic value ($p<0.05$); in addition, type of response (sPR vs. CR) was an independent prognostic factor for OS after adjustment for the type of initial therapy (HR: 0.59; $p=0.009$). Patients who achieved sPR exhibited significantly longer OS compared with those achieving CR (84 months vs. 59 months; $p=0.008$). In the multivariate analysis, RISS was the strongest prognostic factor for OS (HR: 0.32; $p=0.002$).

CONCLUSION: Patients who achieve sPR represent a unique group of NTE MM patients with higher age and favorable prognostic characteristics. Achievement of sPR was a positive prognostic factor for OS, which led to 41% reduction of the risk of death; this latter finding supports that probably therapeutic strategy in NTE MM patients should not always aim at CR, at the expense of toxicity or quality of life.

P48. FIRST REPORT OF AUTOIMMUNE HEMOLYTIC ANEMIA DURING VENETOCLAX THERAPY FOR RELAPSED CHRONIC LYMPHOCYTIC LEUKEMIA

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OBJECTIVE: Autoimmune Hemolytic Anemia is the most frequent autoimmune disorder described in Chronic Lymphocytic Leukemia (CLL) patients with an incidence of 5-10%, however only a minority of patients with positive DAT will develop overt hemolysis. Introduction of therapeutic agents that inhibit intracellular B-cell receptor signaling (ie Ibrutinib, Idelalisib or Venetoclax) has been associated with autoimmune cytopenias but available data need further validation. Venetoclax is a highly selective BCL-2 inhibitor active in relapsed/refractory del (17 p) CLL patients. To our knowledge this is the first case of emerging AIHA reported in the context of single agent therapy with Venetoclax.
Methods: We studied the case of a 73-year old male who was diagnosed in 2013 with CLL Binet stage A. At the time of diagnosis he had no indication for therapy but seven years later he presented with leucocytosis (WBC: 206.070/μL), absolute lymphocyte count (ALC) 97.600/μL, anemia (Hb: 10 g/dL), thrombocytopenia (PLTs: 104.000/μL), massive splenomegaly (maximum diameter: 20 cm) and normal cytogenetics. Bone marrow aspiration revealed 70% infiltration with clonal cells. Direct antiglobulin test (DAT) was positive but no active autoimmune hemolytic anemia (AIHA) was confirmed. The patient was initially treated with cyclophosphamide/fludarabine without response; subsequently he received Ibrutinib which induced complete hematological response, but was suspended six months later due to grade III skin rash. One year later he progressed with excessive lymphocytosis (ALC: 179.990/μL), anemia (Hb: 7 g/dL), thrombocytopenia (PLTs: 68.000/μL) and positive DAT with no active AIHA. Venetoclax was administered orally according to the indicated dose of 20 mg followed by weekly escalation. The patient initially responded but he displayed sudden anemia (Hb: 7,3 g/dL) after dose escalation to 100 mg. We performed a full work up of anemia and a review of literature.
RESULTS: Anemia investigation revealed hemolysis documented by positive DAT, low haptoglobin (0,08 g/L, reference range: 0,3-2 g/L), elevation of lactate dehydrogenase and indirect bilirubin (304 U/L and 2,3 mg/dL respectively, upper limit 250 U/L and 0,9 mg/dL respectively), marked reticulocytosis (113.000/μL) and the presence of spherocytes in the peripheral blood smear. Venetoclax was suspended and the patient fully responded to 1 mg/kg/day prednisolone for 4 weeks (Hb: 12,6 g/dL, haptoglobin: 0,44 g/L, indirect bilirubin: 0,7 mg/dL, lactate dehydrogenase: 250 U/L). A month later Venetoclax was restarted at the dose of 200 mg but the patient displayed again hemolysis and received corticosteroids. Treatment with Venetoclax was suspended, with all values returning to normal.
CONCLUSION: Our patient had positive DAT before treatment initiation and developed AIHA during Venetoclax monotherapy. Hemolysis was displayed during dose escalation from 50 mg to 100 mg, suggesting a possible dose-response relationship. Readministration of therapy at the dose level of 200 mg led to a second AIHA episode. Both hemolytic episodes receded after discontinuation of Venetoclax and treatment with corticosteroids. In our case report, it is difficult to identify whether AIHA was a primary drug-mediated immune event rather than an exacerbation of a pre-existing autoimmune phenomenon in the context of disease activity. Nevertheless, the fact that both AIHA episodes occurred during Venetoclax therapy underlies the need for close monitoring of CLL patients receiving new treatments and highlights the need to acquire more information on the relationship between newer treatments in CLL and AIHA occurring after their use.

P49. POLATUZUMAB-VEDOTIN IN COMBINATION WITH RITUXIMAB/BENDAMUSTINE IN A HELLENIC MULTICENTER COHORT OF RELAPSED/REFRACTORY AGGRESSIVE B-CELL-NON-HODGKIN LYMPHOMA PATIENTS: REAL-LIFE DATA ON EFFICACY & SAFETY

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OBJECTIVE: Salvage chemotherapy and autologous stem cell transplantion (autoSCT) is the standard of care for secondline therapy of relapsed/refractory (RR) Diffuse Large B Cell Lymphoma (DLBCL) patients (pts). However, the majority of pts will be ineligible or will relapse after autoSCT. This group of pts consists an unmet medical need. Polatuzumab Vedotin (Pola), an anti-CD79 b antibody-drug conjugate (ADG), has been recently approved for R/R DLBCL pts, in USA after 2 lines of treatment and in Europe for autoSCT-ineligible pts, in combination with Bendamustine and Rituximab (BR), on the basis of significantly better response rate (RR), progression free survival (PFS) and overall survival (OS), in comparison to BR alone in a randomized Phase 2 trial, GO29365 [Sehn L, et al. J Clin Oncol.38: 155-16,2020]. However, real-life experience with Pola in this setting remains very limited. We present efficacy and safety real-world data on Pola administration in R/R aggressive B-cell non-Hodgkin Lymphoma (B-NHL) pts outside clinical trials.

METHODS: Our cohort consists of adult R/R aggressive B-NHL pts after at least 2 prior treatment lines enrolled in the Greek Companionate Use Program (CUP) of Pola and pts who received Pola according to prescribing information. Pola should be administered in combination with BR or R

alone, if response duration to previous BR was <12 months. The combination should be given for up to six 21-days cycles. Dose schedule was: Pola=1.8 mg/Kg D1, Rituximab=375 mg/m2 D1, Bendamustine=90 mg/m2 D1+2 of each cycle.
RESULTS: Between 03-Oct-2018 and 24-Aug-2020, 53 R/R aggressive B-NHL pts from 19 Hellenic centers were enrolled (44 DLBCL, 4 primary mediastinal LBCL, 3 transformed follicular lymphoma and 2 mantle cell). The median age was 63 years (20-85) and 28 (52.8%) were females. They had received a median of 2 prior regimens (1-8) including ASCT in 17%, while 77.4% were refractory to prior treatment. Pola-BR was administered to 50 pts and Pola-R in 3. The median follow up (FU) time was 6.7 (0.01-14.9) months. Among 52 pts who had completed treatment at the time of the analysis, 21 (40.4%) received all 6 cycles. The median number of cycles given was 4 (1-6). Among 45 pts evaluable for response, RR was 44.4%[CR: 12 (17.6%), PR: 8 (32.4%)]. In 18 of the 20 responders, PET-CT was also performed and in 9 of them it was negative: 20% PET CR. The median PFS was 6.7 months and median OS was 11.4 months. Thirty (30) pts (56.6%) presented an adverse event (AE) grade>=3, the most common being neutropenia and thrombocytopenia (32% and 18.9% respectively). There were 15 fatal events during Pola treatment: 10 due to disease progression and 5 due to AE. Further treatment has been given to 21 pts so far (10 chemoimunotherapy, 6 radiotherapy, 3 lenalidomide,3 ibrutinib, 2 CAR-T cell,1 nivolumab, 1 brentuximab vedotin) and 12 of them are alive, including both CAR-T cell treated pts, after a median time of 8.8 months (3.6-14.9)
Conclusion: Our real-life data confirms that Pola-BR is a promising treatment option for R/R aggressive B-NHL (mainly DLBCL) after 2 lines of treatment. Responses occur even in heavily pretreated pts, with acceptable toxicity.

P50. OUTCOMES OF TYROSINE KINASE INHIBITOR DISCONTINUATION IN ELDERLY PATIENTS WITH CHRONIC MYELOID LEUKEMIA: REAL WORLD DATA FROM A SINGLE INSTITUTION EXPERIENCE

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OBJECTIVE: After the introduction of tyrosine kinase inhibitors (TKIs) most patients with newly diagnosed chronic myeloid leukemia (CML) are considered to have a normal life expectancy. The new challenge for those who display deep molecular response (DMR), is to offer them the perspective of a treatment-free remission (TFR). Our aim was to explore prognosis of elderly CML patients who experience TKIs discontinuation and to record changes in quality of life (QOL) after discontinuation, in the real-world setting.

METHODS: We analyzed the data from the medical records of 7 (M/F: 5/2) CML patients who met criteria for TKIs discontinuation. We recorded the duration of TKI treatment and the duration of DMR before TKIs discontinuation, TFR duration and we evaluated hemoglobin (Hb) levels and EQ-5 D-5 L questionnaire scale before and during TRF.

RESULTS: The median age at the time of discontinuation was 74 years (range 65–88). Median time of duration of TKIs treatment was 13 years (range 5-15); all patients had achieved MR 4.5 for at least 3 years before treatment discontinuation. Three patients were treated with nilotinib and four patients received imatinib before discontinuation. After a median time of observation of 19 months (range 12-22), 6 patients remained in TFR. Only one patient lost MMR, 5 months after discontinuation of treatment and he displayed again MR 4.5 within 4 months after re-initiation of therapy. Regarding the depth of molecular remission 5 patients remained in MR 4,5 and one patient had documented MMR in 2 consecutive measurements; recently, he returned to MR4 without any intervention. During TFR, Hb levels were increased in all six patients (median value: 2.3 gr/dl; range: 0.8-4 gr/dl). Five of them experienced an improvement of EQ-5 D-5 L scores during TFR and only one patient reported a slightly worse QOL due to musculoskeletal pain-related AE during the first 3 months of the TFR phase.

CONCLUSION: Elderly CML patients who have a prolonged duration of treatment before TKIs discontinuation may enjoy a durable TFR. Furthermore, they seem to benefit from treatment discontinuation in terms of anemia that it may be reflected by the ability to perform everyday activities, leading thus to an improvement of QOL.

P51. POSITRON EMISSION TOMOGRAPHY AFTER RESPONSE TO RITUXIMAB-CHOP IN PRIMARY MEDIASTINAL LARGE B-CELL LYMPHOMA: IMPACT ON OUTCOMES AND RADIOTHERAPY STRATEGIES

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OBJECTIVE: In the recent years, end-of treatment (EoT)-PET/CT has been used as a guide to omit radiotherapy (RT) in patients with primary mediastinal large B-cell lymphoma (PMBCL). We evaluated the prognostic significance of PET/CT after response to R-CHOP in PMLBCL aiming to assess (i) the outcome of patients with negative-PET/CT, which might permit the omission of RT (ii) whether RT can provide effective tumor control in PET/CT-positive patients, and (iii) the validity of post-RT PET/CT evaluation, especially regarding the persistence of false-positive results.
METHODS: Among 231 consecutive PMLBCL patients, 182 underwent EoT-PET/CT after at least partial remission to R-CHOP or equivalent regimens, while 49 were not eligible: 18 underwent PET/CT but already had progressive disease (PD), 5 had no PET/CT because of PD, 11 had PET/CT only post-R-CHOP+RT, 14 had no PET/CT (technical reasons), 1 not assessable by D5 PS.
RESULTS: Among 182 patients, 72 (40%), 33 (18%), 28 (15%), 29 (16%) and20 (11%) had D5

PS score (D5 PSS) 1,2,3,4 and 5 respectively. Among patients with D5 PSS-4/5, 34%(10/29) and 95%(19/20) had SUVmax ≥5. The 5-year FFP was 97%,94%,92%,82% and 44% for D5 PSS-1,2,3,4 and 5. Among 105 patients with negative PET/CT (D5 PSS-1/2), 49 (47%) received RT (median dose 3420 cGy) and 56 (53%) did not with relapses in 0/49 vs. 4/56 patients (2 mediastinum and 2 isolated CNS relapses). The 5-year FFP for those who received RT or not was 100% versus 96%, when isolated CNS relapses were censored (p=0.159). Among D5 PSS-3 patients (27/28 irradiated-median dose 3600 cGy) the 5-year FFP was 92%: 11/27 patients had a follow-up PET/CT post-RT: 5/11 converted to PET-negative and 6/11 remained with D5 PSS-3 (only 1/6 progressed). Among the 44/49 patients with positive EoT-PET/CT (D5 PSS-4/5) who received RT (median dose of 4000 and 4400 cGy for D5 PSS-4 and 5), the 5-year FFP for those with SUVmax <5 and ≥5 was 88% and 60% (p=0.065). For D5 PSS-4, 21/28 patients had follow-up PET/CT post-RT: 14/21 converted to PET-negative (2/14 relapsed) and 7/21 remained PET-positive (5/7 remained in remission but post-RT-PET findings downgraded to D5 PSS-3 in 4/5). Finally, 7/15 D5 PSS-5 patients converted to PET-negative with RT (only 2/7 relapsed), while 3/8 patients who remained PET-positive after RT have enjoyed prolonged remissions. All these 3 patients had regression of post-RT PET to D5 PSS-4 or 3, while 4/4 who remained at D5 PSS-5 post-RT progressed.

CONCLUSION: The present study supports the omission of RT in a sizeable fraction of PET/CT-negative patients, which is now evaluated by the IELSG-37 trial. If this is the case, the data presented here in combination with the Vancouver and NCI data raise scientific questions regarding the possibility of RT omission in patients with borderline or potentially false-positive PET/CT. Moreover, our results definitely discourage the use of salvage chemotherapy and ASCT in patients who conventionally respond to R-CHOP, solely based on PET/CT positivity in the absence of documented PD. Finally, a positive PET after RT should not trigger the initiation of further salvage chemotherapy in the absence of conventionally defined PD, with the exception of the persistence of D5 PSS-5 or clearly worsening findings compared to the pre-RT PET/CT evaluation.

P52. SUBCLINICAL COAGULATION DISORDERS IN NEWLY DIAGNOSED PATIENTS WITH HODGKIN LYMPHOMA (HL): A PHENOMENON RELATED TO THROMBOINFLAMMATION

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OBJECTIVE: Considering our observation, that HL-patients frequently present at diagnosis with mild coagulation disorders, we aimed to 1) analyze coagulation parameters [prothrombin time (PT), INR and activated partial thromboblastin time (aPTT)] in newly diagnosed HL patients in comparison to healthy individuals, 2) correlate them with clinical and laboratory parameters, and 3) investigate the possible underlying mechanisms.

METHODS: Coagulation parameters (PT/INR, aPTT, fibrinogen, D-dimers) were determined and recorded in 80 consecutive patients with newly diagnosed HL before treatment initiation, compared to 225 healthy individuals and analyzed according to demographic data, clinical findings (histology, disease extent, IPS, B-symptoms) and laboratory parameters related to inflammation (hemoglobin, platelet and white blood cell count, ESR/CRP, albumin, α2/γ-globulins, ferritin/haptoglobin). Coagulation factors (F) II, V, VII, X and TFPI were measured in plasma and serum with ELISA, respectively, in 35/80 patients.

RESULTS: HL patients demonstrated increased median values of all parameters compared to controls: INR 1.12 vs 0.99 ($p < 0.001$), aPTT 37.8 vs 33.9 ($p < 0.001$) and fibrinogen 587.5 vs 303 ($p<0.001$). INR was elevated (>1.2) in 28.7% of patients, aPTT (>40 sec) in 32.9%, fibrinogen (>400 mg/dL) in 83.3% and D-Dimers (>0.5 μg/ml) in 54.4%. Elevated INR/PT, aPTT, and fibrinogen were observed more frequently in patients with advanced stages (IIB/III/V) and B-symptoms. INR and aPTT correlated strongly with all inflammation markers (Spearman's rho 0.25-0.53 and 0.26-0.38) except of leukocyte counts (and γ-globulins and ferritin for aPTT). Significantly increased levels of FII, FV and FX were observed in the majority of the patients (54.3%-88.6%), while FVII was found to be within normal limits and decreased in 1/35 patients. TFPI levels were also elevated in most cases (65.7%). A negative strong correlation between INR and FVII was noted ($p<0.001$). FII, FV, FX correlated with each other and with fibrinogen ($p= 0.001$-0.030), as well as with inflammation markers. No correlation was found between coagulation factor levels and clinical stage, B-symptoms or IPS, except the one of FX with high IPS ($p=0.039$).

CONCLUSION: Among HL patients 29-33% present with PT/INR and aPTT prolongation at diagnosis, which correlate with advanced stages, B-symptoms, and inflammation markers. This observation is of clinical importance because it prevents further unnecessary investigation. The observed negative correlation between INR and FVII, in combination with the increased levels of TFPI, suggests a possible role of TFPI in terms of excessive inhibition of TF/FVII complex. Notably, the increased levels of FII, FV, and FX correlate with inflammation markers. Taken together, the above data lead to the hypothesis that, prolonged PT/INR and aPTT are collateral findings related to disease activity and raised due to excessive activation of hemostasis in the context of thromboinflammation in HL. Similarly, the elevation of FII, FV, and FX is interpreted within thromboinflammation, which is seemingly in contrast with the prolonged PT/aPTT, suggesting an underlying compensatory mechanism.

P53. COMPARISON OF RITUXIMAB DOSE-ADJUSTED EPOCH (R-DA-EPOCH) WITH RITUXIMAB-CHOP (R-CHOP) CHEMOTHERAPY IN PRIMARY MEDIASTINAL LARGE B-CELL LYMPHOMA (PMLBCL)

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OBJECTIVE: Recent retrospective comparisons revealed modest, non-significant benefit in disease control but much less use of RT with R-da-EPOCH versus R-CHOP. However, the selection of each regimen was at the treating physician's discretion, so that bias was inevitably introduced. We aimed to compare the efficacy and long-term toxicity of R-da-EPOCH versus R-CHOP using much less biased selected control groups (CG) and to investigate the adherence to dose-escalation program according to treatment protocol in real-life clinical practice.

METHODS: In 16 participating Centers in Greece, R-da-EPOCH was adopted at a certain timepoint for all patients with PMLBCL <60 years old (n=86), while R-CHOP had previously been the standard of care. The 1 st R-CHOP CG (CG-1) was selected unbiased from our database among consecutive patients treated at the same Centers, starting from the most recent patient and selecting, if possible, an equal number of R-CHOP-treated patients moving backwards, thus minimizing selection bias. In 5/16 Centers R-CHOP-treated patients selected were fewer than R-da-EPOCH by 13, while 18 patients had received R-CHOP-14. Thus, the core of 55 patients (86-13-18=55) was preserved, while two new R-CHOP CGs were built. In CG-2, the 31 missing patients were substituted by the entire cohort of Nicosia Hospital (n=27). In CG-3, 29 and 2 consecutive patients from 4/16 and from 1 other Center of similar potential to the aforementioned 5 Centers were assigned, respectively. Thus, all 86 patients received R-CHOP-21 and were selected consecutively from a previously generated database.

RESULTS: The R-da-EPOCH (n=86) and R-CHOP CG-1 (n=73), CG-2 (n=82) και CG-3 (n=86) were comparable regarding patient characteristics except for worse PS in R-da-EPOCH group. Two R-da-EPOCH-treated patients developed acute myeloid leukemia (AML) at 10.4 and 22 months from R-da-EPOCH initiation having reached level 6 and 4, respectively. The 5-year freedom from progression (FFP), event-free survival (EFS) and overall survival (OS) were not significantly different (R-da-EPOCH vs R-CHOP CG-1-CG-3 88%vs75-80%, 85%vs73-78%, and 96%vs88-90%). Only a borderline difference in FFP compared to CG-3 was demonstrated (p=0.06). Among patients eligible for consolidative RT (no progressive disease), less R-da-EPOCH patients received RT (14% vs 73%CG-1, 76%CG-2, 58%CG-3). In multivariate analysis, the R-da-EPOCH vs R-CHOP difference in FFP remained non-significant compared to CG-1 and CG-2, but was significant compared to CG-3 [p=0.035, HR=0.40 (0.16-0.94)]. Among 65 patients who completed R-da-EPOCH treatment and had available data, only 40 (61%) received the treatment lege artis. Those patients had 5-year FFP 92% and 55% of them reached level ≥4, in accordance with the NCI study.

CONCLUSION: We report here the least biased comparison between R-da-EPOCH and R-CHOP conducted so far with well-matched subgroups of consecutively treated patients. Although the 5-year FFP and EFS appeared to be less impressive than originally reported by the NCI group and despite the 2 cases of AML, R-da-EPOCH minimized the use of RT in a real-life setting and provided numerically superior disease control than R-CHOP. R-da-EPOCH is not administrated lege artis in a significant proportion of patients, which may affect the efficacy of this regimen.

P54. THE EFFECT SIZE OF ANTI-MYELOMA DRUGS ON SURVIVAL OF ELDERLY MYELOMA PATIENTS; STOCHASTIC ANALYSIS IN A COHORT OF 145 MYELOMA PATIENTS

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OBJECTIVE: Multiple myeloma (MM) is an incurable malignancy occurring after the age of 65 in two thirds of cases. Sequential use of available anti-myeloma drugs is the main strategy of treatment. In this real world retrospective study we are checking the effect size of anti-myeloma drugs on myeloma relapse free survival time by using a stochastic approach.
METHODS: In the semi Markov model that we constructed, the states are the four treatment regimens: Bortezomib, Lenalidomide, Chemo/TLD and the Combinations of novel agents (daratumumab, carfilzomib, ixazomib, pomalidomide based regimens). Furthermore, the transition time is considered the time from one drug regimens to its successor, which is actually the TTNT in months. In order to construct the Semi Markov model we identify the distributions of the time (TTNT) and also we construct the stochastic matrix with the probabilities.
RESULTS: As expected after lenalidomide treatment 52% of patients switched to bortezomib based regimens and after bortezomib 48% received lenalidomide. In patients relapsed after thalidomide and chemo 40% received bortezomib and 40% received lenalidomide based regimens. Combinations of new agents (Daratumumab, Carfilzomib, Ixazomib and pomalidomide) were used in 32% of patients after treatment with bortezomib and in 21% of patients treated with lenalidomide. In subsequent relapses after novel agents' combination the vast majority of patients received another novel agent combination (80%) while the rest 20% received chemotherapy with DPACE regimen. One of the basic questions in stochastic models of analysis is to compute the mean of time in each state (residence time). The mean time for the states (drug regimens) is the mean of TTNT from one treatment to the next one. We computed only the mean of TTNT for bortezomib and lenalidomide including all lines of therapy (due to lack of enough values for the other states) and the mean residence time for lenalidomide was significantly longer compared to bortezomib 29,29 months vs 18,526 months.
CONCLUSION: Our stochastic model shows that patients had equal probabilities to receive all available drugs and elderly myeloma patients had median residence (TTNT) on oral treatments with lenalidomide longer compared to bortezomib containing regimens.

P55. TREATMENT AT BIOCHEMICAL RELAPSE AND ABSENCE OF DEL17 P ARE RELATED WITH BETTER OS AFTER FIRST RELAPSE OF MULTIPLE MYELOMA PATIENTS; REAL WORLD DATA FROM A SINGLE CENTER IN A COHORT OF 140 RRMM.

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OBJECTIVE: Improvements in frontline treatment of multiple myeloma (MM) resulted in most of the patients to achieve deep and durable responses. Nevertheless, even patients achieving complete responses (CR) finally relapses.
METHODS: Herein, we retrospectively study the effect of relapse clinical features on OS in a cohort of 140 RRMM patients diagnosed in a single center from January 2005 till December 2019.
Results: This cohort entailed 140 MM patients at first relapse 76 men and 64 women and among them 60 were transplant eligible (TE) and 80 were non- transplant eligible (NTE) by intention to treat (ITT) at diagnosis. Among TE patients 27 relapsed after receiving autologous transplant as first line treatment and 33 relapsed without receiving autologous transplant. Focusing in TE only patients OS after relapse was statistically equal either if they had received autologous transplant at first line or not [Median OS ASCT Yes: 45,5 months (31,2-59,3) and ASCT NO: 50,3 (29-71,5), Long Rank p=0,692]. Thirty-eight patients were treated at biochemical relapse and 98 were treated at clinical relapse. Median Progression Free survival (PFS) after first relapse was 22 months (18,5-25,5) for Biochemical relapsed patients and 12 months (7,6-17) for those treated at clinical relapse (Long Rank p=0,103). Median Overall Survival (OS) after first relapse was statistically superior for patients treated at biochemical relapse compared to those treated at clinical relapse [mOS Biochemical Relapse: 55 months (45-65,8) vs Clinical Relapse: 26 months (23-26,6), Long Rank p=0,013]. Afterwards, we included only patients that relapsed after achieving more that partial remission to previous therapy and we separated them according to time of relapse. Forty-eight patients relapsed in less than 12 months from start of first line therapy and 69 relapsed in more than 12 months after starting first line treatment. Survival rates were the same between these two groups [Median OS after relapse for Relapse < 12 months: 41 months (29,6-52,6) and for Relapse > 12 months: 38,3 months (28-48,3), Long Rank p=0,724]. Then we compared survival after relapse according to clinical characteristics at relapse. In our cohort 77 patients had renal impairment at relapse and 55 patients had normal renal function. Extramedullary disease (EMD) at relapse occurred in 33 patients while 100 had not extramedullary plasmocytomas. Cytogenetic analysis at relapse was performed at 45 patients and 37 had standard risk cytogenetics and 8 had high risk cytogenetics (del 17 p). In Cox regression multivariate Hazard risk analysis neither renal impairment (Long Rank p=0,138) or EMD were important for overall survival (Long Rank p=0,068) but on contrary high risk cytogenetics had HR for death: 6,415 (1,832-22,467) and Long Rank p=0,04.
CONCLUSION: In conclusion, relapsed patients had better survival if they were treated at biochemical relapse instead of those treated at clinical relapse. Time of relapse (less than 12 months or not) or relapse after ASCT are not important prognostic factors for survival after relapse. Renal impairment and EMD at relapse are not of prognostic significance at relapse in contrast to high risk cytogenetics that defines a group with extremely poor prognosis.

P56. COVID-19: JUST AN INFECTIOUS DISEASE? OR A POTENTIAL DEBILITATING DISASTER?

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INTRODUCTION: The disease caused by SARS-CoV-2, coronavirus disease 2019 (COVID-19), presents flu-like symptoms which can become serious in high risk individuals. It has shown that hospitalized patients with hematological cancers have similar infection rates but more severe disease and case fatality rates and also confirmed for patients with multiple myeloma (MM) in other study. Patients with MM are susceptible to viral and bacterial infections with approximately 7-10-fold higher risk. Compromised immune system due to both the disease and anti-myeloma therapies is the main predisposing factor. Here, we report a case of COVID-19 in a patient with MM who successfully treated with the humanized anti-IL-6 receptor antibody tocilizumab, but later on developed evident pulmonary fibrosis.

CASE PRESENTATION: A 67-year-old woman who had a history of symptomatic MM, developed overt dyspnea with fever and cough on 28 April 2020. She received 4 cycles of induction chemotherapy consisting of bortezomib, cyclophosphamide and dexamethasone. Very good partial response was achieved after 4 cycles. She was not a bone marrow transplantation candidate therefore maintenance therapy with weekly bortezomib and dexamethasone was decided to give. On the third week of maintenance therapy she administered with respiratory symptoms. Computed tomography (CT) imaging of chest showed multiple ground-glass opacities and patchy consolidation in both lungs (Figure 1 A-B-C). Nasopharyngeal swab specimens were collected to detect SARS-CoV-2 nucleic acid. The swab specimens were tested by real-time reverse transcriptase-polymerase chain reaction; a positive result was received 3 days later. The patient was diagnosed with COVID-19, and was given 200-mg hydroxychloroquine tablets BID orally, and respiratory therapy. But the patient's chest tightness was aggravated with shortness of breath as a result of decreased arterial oxygen saturation (~92% at rest). She was immediately transferred to intensive care unit. The patient's illness was evaluated as severe. Considering her sustained shortness of breath, 40 mg of methylprednisolone, administered IV daily, was given on days 4 to 8. Laboratory investigations revealed a high level of serum CRP, d-dimer, fibrinogen and sedimentation. Liver enzymes were elevated around to 4-fold of the upper limit of normal reference range. On hospital day 5, the patient was given 8 mg/kg tocilizumab, administered IV, once a day. On hospital day 14, her chest tightness disappeared. After tocilizumab administration, CRP, sedimentation and d-dimer levels decreased gradually over the following days. On hospital day 21 the patient had a second chest CT scan, which showed that the range of ground-glass opacities were almost decreased but extensive fibrotic involvement was developed (figure 1 D/E/F). The patient was discharged from the hospital on day 25. Laboratory findings have settled down, severe dyspnea and shortness of breath were resolved. But exertional dyspnea came into prominence. Pulmonary function test showed restrictive lung disease with low forced vital capacity (FVC). Anti-myeloma therapy was started after 2 months delay. The patient had recovered from COVID-19 with a lifelong debilitating morbidity; pulmonary fibrosis.

DISCUSSION: To date, about 15.5 million people worldwide have recovered from COVID-19, but there remains concern that some organs, especially lungs, might have long-term impairment following infection. In inflammatory lung disorders, such as those associated with autoimmune disease; advancing age and severity of inflammation are risk factors for the development of pulmonary fibrosis (4). Progressive, fibrotic irreversible interstitial lung disease, which is characterised by declining lung function, increasing extent of fibrosis on CT, worsening symptoms and quality of life, and early mortality. The burden of pulmonary fibrosis after COVID-19 recovery could be substantial.

At present, the long-term pulmonary consequences of COVID-19 remains speculative and should be reviewed with prospective randomised studies.

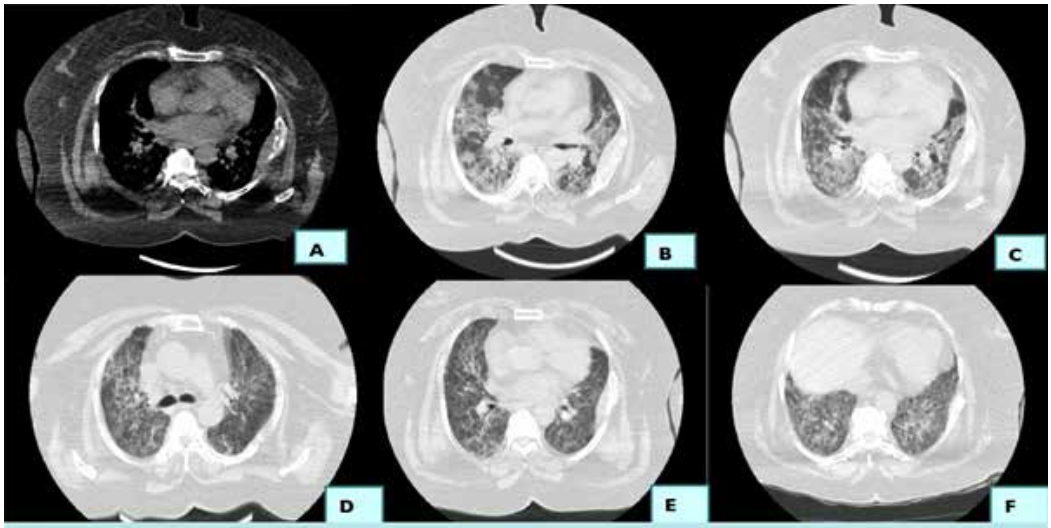

Figure 1: Lung CT of a patient with coronavirus disease 2019
A-B-C: Images of multiple ground-glass opacities and patchy consolidation in both lungs
D-E-F: Three weeks later, at the same lung zones, the disease has rapidly progressed and fibrotic changes are now evident