Balkan Myeloma Study Group

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BOOK OF ABSTRACTS

ORAL PRESENTATIONS

01. REAL-WORLD EFFECTIVENESS AND FACTORS ASSOCIATED WITH RESPONSE TO THROMBOPOIETIN RECEPTOR AGONISTS IN IMMUNE THROMBOCYTOPENIA: RESULTS FROM A GREEK NATIONAL REGISTRY

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OBJECTIVE: Thrombopoietin receptor agonists (TPO-RAs) are effective in the treatment of persistent and chronic primary immune thrombocytopenia (ITP). However, few studies have evaluated their long-term effectiveness and predictors of response.

METHODS: We conducted an analysis of data from a multicenter, retrospective, nationwide Greek registry of adult patients with primary ITP who had received TPO-RAs, to assess parameters associated with response. Response was defined according to the International Working Group criteria. Written informed consent was obtained from all participants, and the study was approved by the Scientific Committees of the participating centers.

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RESULTS: A total of 317 patients from 14 centers were included (38.7% male; median age, 60 years). Prior to TPO-RA treatment, patients had received a median of 2 (0-5) treatment lines (95.9% corticosteroids ± intravenous immunoglobulin). Eltrombopag was selected in 68.1% of patients, followed by romiplostim (21.1%) and avatrombopag (10.4%). The median time from diagnosis to TPO-RA initiation was 8.0 (0.0-532.0) months. The main indications for TPO-RA initiation were corticosteroid dependence (64.5%), recurrent bleeding (25.9%), steroid intolerance (4.8%), and use as first-line treatment (4.8%). Response was achieved in 82.0% of patients [complete response (CR), 67.4%; response (R), 14.6%] and was not associated with the number of previous treatments, any individual previous treatment, or the TPO-RA used. In contrast, a higher platelet count (PLT) before TPO-RA initiation was associated with response ($p<0.001$). The median time to CR was 1 month and to R 1.8 months, and were not associated with sex, age, Bleeding Assessment Tool (BAT) score, PLT count before TPO-RA initiation, or the TPO-RA administered. In contrast, a longer time to response was associated with a longer interval from diagnosis to treatment initiation ($p=0.004$), a greater number of treatment lines (0 or 1 vs >1, $p=0.026$), and previous treatment with IVIG ($p=0.015$) or splenectomy ($p=0.029$), but not with rituximab or other immunosuppressive therapy. Overall, 21.8% of patients discontinued treatment because of sustained CR. Among these patients, relapse occurred in 33.3%. The median treatment-free remission (TfR) was not reached. Most relapses occurred within the first two years after treatment discontinuation, whereas patients who remained relapse-free beyond two years did not relapse. TfR was not associated with sex, age, number of treatment lines, or TPO-RA indication for TPO-RA. Longer TfR was observed in patients with a BAT score >1 at diagnosis ($p=0.018$).

CONCLUSION: This is one of the largest registries worldwide of patients with ITP treated with TPO-RAs. The analysis showed that TPO-RAs resulted in a response in >80% of patients (CR 67,4%), irrespective of the TPO-RA used. Responses were rapid but were affected by multiple previous treatments, while time to CR was longer in patients with longer disease duration. Treatment discontinuation after sustained CR was feasible in a substantial proportion of patients, while TfR was not significantly associated with the main baseline patient characteristics. The findings of this study complement those of prospective discontinuation studies and other retrospective registries and indicate that prolonged treatment-free responses can be achieved in a substantial proportion of patients, while late relapses are uncommon.

02. PRE-LYMPHODEPLETION RNA SEQUENCING REVEALS ENDOTHELIAL-IMMUNE SIGNATURES OF CAR T-CELL TOXICITIES AND MORTALITY: A PROSPECTIVE TRANSLATIONAL STUDY

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OBJECTIVE: Chimeric antigen receptor (CAR) T-cell therapy has revolutionized the therapeutic outcomes of patients with relapsed/refractory (R/R) hematological malignancies. However, cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) remain major toxicities. Endothelial injury and thromboinflammation are considered established contributors to their pathogenesis. Still, the pre-infusion transcriptional background that may predispose patients to the aforementioned toxicities remains poorly characterized. Thus, we investigated whether pre-lymphodepletion immune-endothelial transcriptional profiles can identify distinct signatures associated with CAR T-cell toxicities and post-infusion mortality.

METHODS: In this prospective translational cohort study, consecutive adult patients who received CAR T-cell therapy for R/R hematologic malignancies at our JACIE-accredited center were enrolled. Peripheral whole-blood samples were collected before lymphodepleting chemotherapy, and peripheral blood mononuclear cells (PBMCs) were isolated. Targeted RNA sequencing was performed using a custom endothelial injury and inflammation-associated 75-gene panel, with 73 genes retained after primer validation. Patients were prospectively monitored for grade 2-4 CRS and ICANS, according to ASTCT criteria, isolated and concurrent toxicity, and mortality. Differential expression, hierarchical clustering, principal component analysis (PCA), UpSet analysis, and functional enrichment were performed. Survivors without grade 2-4 toxicity (n=10) served as the internal reference for mutually exclusive phenotypes.

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RESULTS: We studied 45 patients; 31 (68.9%) developed grade 2-4 CRS, 7 (15.6%) developed grade 2-4 ICANS, and 6 (13.3%) developed concurrent toxicity, while 8 (17.8%) died during a median follow-up of 12.0 months. Across six comparisons, 36 unique differentially expressed genes (DEGs) were identified. Specifically, overall CRS yielded 14 DEGs; TIMP1 downregulation remained significant after false discovery rate (FDR) adjustment (q=0.009), along with BUB1/TK1 upregulation and LILR-family suppression. Isolated CRS showed the strongest signature (18 DEGs): TIMP1 was downregulated (q=0.008), MPO and BUB1 were upregulated (both q=0.011), cell-cycle genes were activated, and LILRs were suppressed. Overall, ICANS yielded three nominal DEGs (PLSCR1 upregulated, FCGR3B upregulated, GAB2 downregulated), but none were significant after FDR adjustment. Moreover, isolated ICANS was associated with a nine-gene, complement-related pattern (C1QA/B/C upregulated). Concurrent grade 2-4 CRS/ICANS was characterized by 12 DEGs, combining MPO, cell-cycle, and C3AR1 upregulation with TIMP1/LILRA6/LILRB2 downregulation. Mortality yielded 11 DEGs, dominated by a paradoxical downregulation of MPO (q=0.000052), with decreased BUB1/GPD2/BPGM/DDX6 and increased EPSTI1 expression. No death was directly attributed to CRS or ICANS alone. Hierarchical clustering resolved five functional clusters: immune activation/inhibitory receptors, cell cycle/proliferation, proteolytic remodeling, oxidative stress, and metabolic/epigenetic regulation, with progressive dysregulation from the reference group to isolated CRS and concurrent toxicity. PCA showed partial separation for CRS and mortality but minimal separation for ICANS. Moreover, enrichment analysis implicated DNA replication and antigen processing in isolated CRS, complement/humoral immunity in isolated ICANS, and immunoregulation/neutrophil degranulation in concurrent toxicity.

CONCLUSION: Based on our findings, pretreatment PBMC transcription analysis captured a shared and toxicity-specific endothelial-myeloid vulnerability before CAR T-cell infusion. Following multicenter external validation, a compact blood-based panel could complement clinical tools such as Endothelial Activation and Stress Index for early patient risk stratification. Nevertheless, longitudinal studies should determine whether these transcriptional signatures may also predict long-term outcomes, particularly prolonged hematotoxicity, infections, and therapy-related myeloid neoplasms.

03. THE COMBINATION OF LOW-DOSE POST-TRANSPLANT CYCLOPHOSPHAMIDE WITH LOW-DOSE ALEMTUZUMAB IS ASSOCIATED WITH REDUCED RATE OF CHRONIC GVHD AFTER MATCHED UNRELATED DONOR TRANSPLANTATION

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OBJECTIVE: Post-transplant cyclophosphamide (PTCy) has been increasingly used for the prevention of graft-versus-host disease (GvHD) after allogeneic stem cell transplantation (allo-HSCT). However, its use is associated with delayed neutrophil engraftment and increased risk of opportunistic infections. Thus, the optimal PTCy dose and the ideal combination of immunosuppressants remain uncertain. The aim of this study was to evaluate the outcomes after matched unrelated (MUD) allo-HSCT, using reduced-dose PTCy, with reduced-dose alemtuzumab.

METHODS: We retrospectively analyzed 47 patients undergoing MUD allo-HSCT at a single center. GvHD prophylaxis consisted of either PTCy 25mg/kg, on days +3/+4, alemtuzumab 5mg on days −2/−1 and calcineurin inhibitor (alemtuzumab/PTCy-group, 29 patients) or PTCy 25mg/kg, on days +3/+4 and a calcineurin inhibitor with MMF (PTCy group, 18 patients). Outcomes included acute and chronic GVHD (aGVHD, cGvHD), relapse, non-relapse mortality (NRM), overall survival (OS), and GVHD- and relapse-free survival (GRFS).

RESULTS: Forty-seven patients (25 males and 22 females) were included in the study. Median age was 27 years (range, 19-66). 13 patients had active disease. Donor was >30 years-old in 20 patients and <30 years-old in 27 patients. In 8 cases, there was a female-donor to male-recipient. 40 patients had DPB1-mismatch (19 non-permissive). At a median follow-up of 14 months, the cumulative incidence (CI) of aGvHD grade II-IV was 34% (21%-47%). No difference was observed in the CI of aGvHD between the PTCy and the Alemtuzumab-PTCy group (p=0.23). Chronic GvHD of any grade occurred in 24 patients (51%), including moderate-to-severe cGvHD in 13 (28%). At 2-years after transplantation, the CI of moderate-to-severe cGvHD was significantly lower in the alemtuzumab/PTCy-group [11% (95% CI, 3%-25%)], as compared to the PTCy-group [63% (95% CI, 29%-83%], (p<0.001), which remained significant after adjusting for donor-age and for female-donor-to-male-recipient sex mismatch (p<0.001). At 1-year after transplantation, the CI of NRM was 14%, with no difference between the alemtuzumab/PTCy- and PTCy-groups (p=0.8). In a multivariate analysis, no factor (alemtuzumab, donor age, female-donor-to-male-recipient) was found to be associated with NRM. The CI of relapse was 20% (95% CI, 8%-37%) in the PTCy-group and 5.5% (95% CI, 1%-22%) in the alemtuzumab/PTCy-group, although this difference was not significant (p=0.1). At 2-years after transplantation, the OS was similar between the PTCy- [80% (95% CI, 50%-93%)] and the alemtuzumab/PTCy-group [75% (95% CI, 56%-88%)], (p=0.8). The GRFS was significantly higher in the Alemtuzumab/PTCy-group [84% (95% CI, 61%-94%)], compared to the PTCy-group [22% (95% CI, 4%-49%)], (p<0.001). CMV reactivation occurred in 8/47 (17%) patients, whereas haemorrhagic cystitis was reported only in 4/47 patients (grade 1-2). The median neutrophil and platelet engraftment was 13 days (range, 10-20) and 11 days (range, 7-23), respectively.

CONCLUSION: In this retrospective study of patients undergoing MUD allo-HSCT, reduced-dose PTCy-based prophylaxis was associated with very encouraging relapse, NRM and survival outcomes. The addition of alemtuzumab to PTCy was associated with a marked reduction in moderate-to-severe cGvHD and a substantial improvement in GRFS, without an adverse effect on relapse and OS. Larger, multicentre studies, with longer follow-up are required to confirm the results.

04. REAL-WORLD CLINICAL UTILITY OF NEXT-GENERATION SEQUENCING IN PHILADELPHIA-NEGATIVE MYELOPROLIFERATIVE NEOPLASMS

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OBJECTIVE: Next-generation sequencing (NGS) has become increasingly integrated into the management of Philadelphia chromosome-negative myeloproliferative neoplasms (MPNs). Growing knowledge of the molecular landscape of MPNs is being combined with existing prognostic models based on clinical, laboratory, and cytogenetic information. These molecular-based prognostic models enable the creation of personalized treatment strategies, improving overall survival for patients with MPNs.

METHODS: We retrospectively evaluated consecutive patients with Philadelphia chromosome-negative MPNs who underwent NGS analysis at our tertiary referral center. Demographic characteristics, disease subtype, driver mutation status, cytogenetic findings, indications for NGS testing, detected mutations, prognostic risk scores, and subsequent treatment modifications were reviewed. Disease-specific prognostic models, including MIPSS70, DIPSS-Plus, MIPSS-PV, MIPSS-ET, Triple A, and IPSET-Thrombosis, were applied when appropriate.

RESULTS: A total of 22 patients with Philadelphia chromosome-negative MPNs underwent NGS. The cohort included 7 primary myelofibrosis, 6 polycythemia vera, 4 essential thrombocythemia, 3 post-ET myelofibrosis, and 2 post-PV myelofibrosis patients. The median age was 61 years (range, 44-81), and 12 (54.5%) were female. Among patients tested, JAK2 V617F mutation by PCR was detected in 14/19 (73.7%), CALR mutation in 4/10 (40%), whereas no MPL mutation was identified by PCR. Conventional cytogenetics showed a normal karyotype in 15 patients; trisomy 8 (n=2), trisomy 9 (n=1), and loss of chromosome Y (n=1) were observed in the remaining patients. FISH confirmed chromosome 9 abnormality in the patient with trisomy 9. NGS was requested for evaluation of disease progression in 11 patients (50%), prognostic assessment in 10 (45.5%), and diagnostic clarification in one (4.5%). At the time of analysis, NGS results were available for 16 patients. The detected mutations were JAK2 V617F (n=8), CALR (n=4), ASXL1 (n=3), TET2 (n=2), SH2B3 (n=2), DNMT3A (n=2), NRAS (n=2), SRSF2 (n=1), and MPL (n=1). Six patients harbored two or more pathogenic mutations. Among 12 patients with myelofibrosis, MIPSS70 classified 2 patients as low-risk, 7 as intermediate-risk, and 2 as high-risk, while DIPSS-Plus classified 2 as low-risk, 6 as intermediate-1, and 4 as intermediate-2. Among six PV patients, MIPSS-PV classified three as low-risk and two as intermediate-1. Among four ET patients, all were classified as intermediate-1 according to the Triple A score, whereas IPSET-Thrombosis categorized three as intermediate-risk and one as high-risk. NGS findings resulted in changes in therapeutic strategy in 6/22 patients (27.3%), including referral for allogeneic hematopoietic stem cell transplantation (n=2), planned addition of selinexor to JAK inhibitor therapy before transplantation (n=1), initiation of hydroxyurea (n=2), and switching from hydroxyurea to ruxolitinib (n=2).

CONCLUSION: Next-generation sequencing appears to be a valuable adjunct to conventional clinical and prognostic assessment in patients with Philadelphia-negative myeloproliferative neoplasms, with the potential to influence individualized treatment strategies. Given the limited sample size and the heterogeneity of disease subtypes, larger multicenter real-world studies are needed to establish standardized indications for NGS and to determine its impact on clinical decision-making and patient outcomes.

05. THE TRANSCRIPT MATTERS: COMPARING MOLECULAR RESPONSE AND TREATMENT-FREE REMISSION IN E13A2- AND E14A2-POSITIVE CML

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OBJECTIVE: Chronic myeloid leukemia (CML) is defined by the BCR: ABL1 fusion gene, with e13a2 and e14a2 being the two most common p210 transcript variants. Although these transcripts were historically considered equivalent, evidence suggests that they may differ in biological behavior, molecular response kinetics, treatment requirements, and treatment-free remission (TFR) outcomes. This study compared baseline disease features, molecular responses, treatment changes, TFR outcomes, and overall survival (OS) between patients with these transcripts.

METHODS: We conducted a comparative analysis of 132 patients with CML (53 patients with e13a2, 79 with e14a2). Baseline white blood cell (WBC), platelet counts, Hasford/EUTOS/ELTS scores, achievement and time to major and deep molecular response (MMR and dMR), treatment changes, TFR eligibility, TFR duration, and OS were evaluated between groups. The number of patients analyzed varied according to the availability of data for each outcome. Continuous variables were summarized as means and compared using independent-samples t-tests. Categorical variables were compared using chi-square or Fisher's exact tests. A two-sided $P<0.05$ was considered statistically significant.

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Results: Patients with e13a2 were older at diagnosis than those with e14a2 (52.2 vs. 49.2 years; P=0.284) and had higher mean WBC counts (116.4 vs. 107.9×10^9/L; P=0.650) but significantly lower mean platelet counts (345.4 vs. 610.3×10^9/L; P<0.001). e14a2 patients achieved MMR more frequently than e13a2 patients (100.0% [53/53] vs. 89.9% [71/79]; P=0.021), although mean time to MMR was not significantly different (16.2 vs. 18.2 months; P=0.650). dMR was also achieved more frequently in the e14a2 group (94.3% [50/53] vs. 81.1% [60/74]; P=0.036), whereas mean time to dMR did not differ significantly (29.1 vs. 41.3 months; P=0.182). Patients with e13a2 required more treatment modifications than those with e14a2 (0.71 vs. 0.60 changes; P=0.497). Among patients who discontinued TKI therapy, TFR success was higher in the e14a2 group (66.7% [4/6] vs. 60.0% [3/5]; P=1.000), while TFR duration was comparable (31.6 vs. 33.7 months; P=0.884). OS was similar, with survival rates of 95.5% (64/67) for e13a2 and 98.0% (49/50) for e14a2 (P=0.635) and comparable mean survival durations (128.5 vs. 127.4 months; P=0.951). Risk-score distributions were comparable between transcript groups. Hasford low-, intermediate-, and high-risk categories occurred in 60.3%, 34.9%, and 4.8% of e13a2 patients versus 68.5%, 29.6%, and 1.9% of e14a2 patients, respectively (P=0.528). EUTOS low- and high-risk categories occurred in 95.3% and 4.7% of e13a2 patients versus 90.7% and 9.3% of e14a2 patients (P=0.538). ELTS low-, intermediate-, and high-risk categories occurred in 70.9%, 23.6%, and 5.5% of e13a2 patients versus 76.1%, 19.6%, and 4.3% of e14a2 patients (P=0.842). Therefore, superior MMR and dMR rates in the e14a2 cohort cannot be explained by a more favorable baseline risk profile.

CONCLUSION: e14a2 transcript was associated with more favorable molecular outcomes, fewer treatment modifications, higher TFR success than e13a2, but survival was similar. The transcript effect on prognosis appeared independent of risk scores. These findings suggest that transcript type may be useful for response monitoring and TFR counseling, although treatment selection, subsequent therapy, and patient-related factors may influence outcomes. Prospective studies are needed to clarify its prognostic and treatment-predictive value.

06. CLINICAL AND MOLECULAR RISK STRATIFICATION IN SYSTEMIC MASTOCYTOSIS: PROGNOSTIC PERFORMANCE OF IPSM, MARS AND MAPS IN A MULTICENTER REAL-WORLD COHORT

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OBJECTIVE: Systemic mastocytosis (SM) is a rare clonal mast cell neoplasm with heterogeneous clinical behavior. IPSM provides clinical risk stratification, while NGS-based models (MARS and MAPS) incorporate adverse molecular features. The concordance and prognostic relevance of these tools in real-world remain incompletely defined. We assessed the concordance of these scores and their association with outcomes in a multicenter cohort of patients with SM.

METHODS: We conducted a retrospective, observational study of SM patients from three centers in Greece. Patient data at diagnosis were retrospectively collected from institutional records. IPSM was assessed according to disease category, while MARS and MAPS were evaluated in patients with advanced SM for whom the required clinical and molecular data were available. Survival probabilities were estimated using the Kaplan-Meier method and compared using the log-rank test.

RESULTS: Sixty-five patients were included; 40 with non-advanced SM and 25 with advanced SM (ASM n=14, SM-AHN n=9, MCL n=2). Advanced SM patients were older at diagnosis (mean age 57.1 vs. 42.6 years) and had higher serum tryptase levels (median 75.0 vs. 46.4 ng/mL) and greater bone marrow mast-cell infiltration (mean 21.0% vs. 15.0%) than patients with non-advanced SM. S/A/R mutations were identified in 20% of patients with advanced SM and were not detected in the non-advanced cohort. Among patients with advanced SM, higher IPSM was associated with shorter overall survival(OS) (log-rank p=0.0035; HR 6.31 per category increase, 95% CI 1.94-20.51; p=0.0022), with median OS of 104.0, 30.0, 2.5 months for AdvSM-2, AdvSM-3, AdvSM-4, respectively. MARS showed a similar prognostic gradient (log-rank p=0.0361; HR 3.32 per category increase, 95% CI 1.14-9.67; p=0.0278), with median OS of 55.0, 22.0, 19.0 months for low-, intermediate-, high-risk groups, respectively. MAPS showed a trend toward inferior survival with increasing risk category, but did not reach statistical significance (log-rank p=0.1879). Notably, the presence of an associated myeloid neoplasm was strongly associated with adverse outcomes. Patients with SM-AMN had a median OS of only 6 months compared to 55 months in patients with ASM/MCL without AMN (log-rank p=0.0458). In Cox analysis, SM-AMN was associated with a nearly four-fold higher risk of death, however, statistical significance was not reached (HR 3.93, 95% CI 0.93-16.65; p=0.0634).

CONCLUSION: In this real-world multicenter cohort, IPSM and MARS demonstrated significant prognostic impact in advanced SM, while MAPS showed a similar but non-significant trend. Importantly, the presence of an AMN emerged as a major adverse prognostic feature dramatically affecting survival. These findings highlight the prognostic significance of the myeloid disease component and support the need for integrated clinical and molecular risk assessment which would define the optimal therapeutic approach. Larger cohorts and longitudinal follow-up are warranted to confirm these observations. Our perspective is to perform NGS and analyze data from all 194 patients currently included in the Greek Registry.

07. CLONAL HEMATOPOIESIS IN AUTOLOGOUS GRAFTS FROM PATIENTS WITH MULTIPLE MYELOMA UNDERGOING AUTOLOGOUS STEM CELL TRANSPLANTATION

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PURPOSE: Autologous stem cell transplantation (ASCT) remains the standard of care for eligible patients with newly diagnosed multiple myeloma (MM). Clonal hematopoiesis (CHIP) is defined by the presence pathogenic somatic mutations in "driver" myeloid genes in peripheral blood and/or bone marrow without any related cytopenias, dysplasia or myeloid hematologic malignancy. The purpose of the present study was the investigation of possible CHIP and its significance in samples of autologous stem cell grafts from patients with MM, since these patients are usually of relatively older age, have received prior treatment and have been subjected to the stress of stem cell mobilization.

PATIENTS AND METHODS: 109 MM patients who underwent ASCT between 2013 and 2024 have been retrospectively analyzed on the basis of graft sample availability. Patients had complete disease evaluation at diagnosis, before and after ASCT. Patients were subjected to induction treatment, mobilization and stem cell collection and subsequently received high dose melphalan and ASCT. DNA was extracted from cryopreserved samples from autologous grafts and the presence of CHIP-related mutations was studied with next generation sequencing (NGS). Results with variant allele frequency (VAF) ≥1% were considered positive. Notably, samples with VAF of the mutated gene ~50% were not rejected as negative, if the corresponding mutations were not classified as "non-malignant or "possibly non-malignant" from genome databases.

RESULTS: Patient's median age at diagnosis was 59 years (35-72), 47% were male and the median follow-up time was 41.5 months (0.5-126.6). The majority (92.5%) received bortezomib-based induction treatment. Mutations in at least one of CHIP-related gene (CHIP+) were found in 56.9% of patients with the most frequent being ATM (16.5%), MPL (10.1%), TET2 (10.1%), DNMT3A (9.2%), IKZF3 (5.5%) and JAK2 (4.6%). Median overall survival (OS) was 99.6 months and 5-year OS was 83% for the whole population. There was a trend for inferior OS for CHIP+ patients, however this difference was not statistically significant. When individual genes were analyzed, OS was significantly inferior for patients with DNMT3A mutations (p= 0.005), and DNMT3A and/or IKZF3A mutations (p= 0.006). Regarding hematopoietic reconstitution after ASCT, platelet recovery on day +30 and +100 differed significantly between CHIP+ and CHIP- patients (p=0.006 and 0.04, respectively).

CONCLUSIONS: Our study provides new information regarding the presence of CHIP in autologous stem cell grafts in >50% of MM patients. The presence of CHIP correlates with platelet reconstitution after ASCT, while specific driver gene mutations seem to be associated with overall survival after ASCT. Given the multiple lines of therapy that MM patients are subjected to, during the natural course of the disease, caution should be taken about the possible clonal evolution of CHIP.

08. INDEPENDENT COHORT VALIDATION OF THE IMWG 20/2/20 AND PANGEA 2.0 RISK STRATIFICATION MODELS FOR PATIENTS WITH SMOLDERING MULTIPLE MYELOMA (SMM)

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OBJECTIVE: Evaluation of the risk of progression to symptomatic disease is crucial for the follow-up and management of patients with smoldering multiple myeloma (SMM). The International Myeloma Working Group (IMWG) 20/2/20 prognostic model stratifies SMM patients into three prognostic subgroups providing a static image. The Pangea 2.0 model incorporate additional variables to provide a more individualized risk assessment incorporating dynamic predictions. We evaluated both models in an independent cohort of SMM patients.
METHODS: We analyzed consecutive SMM patients diagnosed at our center, using the IMWG 2014 criteria. All patients had a bone marrow (BM) biopsy at diagnosis. Patients were classified according to both the IMWG 20/2/20 and Pangea 2.0 risk stratification models (with and without BM) using clinical and laboratory parameters available at diagnosis. Median follow up was 3 years.
RESULTS: A total of 394 patients were included, (median age of 64.5 (IQR: 56.25-74); 53.8% were females; 69.9%, 25.13% and 4.31% were IgG, IgA and light chain only SMM, respectively. Median BM infiltration was 15% (IQR: 10-20) while the median M-protein concentration was 1.1 g/dL (IQR: 0.70-1.62). During a median follow-up of 3 years, 52 (13.2%) patients progressed to symptomatic multiple myeloma; the 1- 2- and 3- year cumulative progression was 2%, 8% and 10% for the whole cohort. Per the 20/2/20 model, 62% of patients were low, 26% intermediate and 12% high-risk. The 2-year cumulative progression rate was 1.6%, 6.4%, and 14.7%, for low, intermediate and high-risk patients, respectively, ($p<0.001$) suggesting an 11-fold higher risk of progression for high vs. low-risk groups (HR:11) and a ~6-fold higher for intermediate vs low-risk patients (HR:6, $p<0.001$), while the risk of progression for high vs intermediate-high risk groups was ~2 fold (HR:2.3, $p=0.011$). The model demonstrated satisfactory discrimination (C-index of 0.777) and a satisfactory explained variation (R2 =0.113). The Pangea 2.0 model with BM data, provided a more individualized prediction of the 2-year progression risk and 18% were classified as having ≤2% probability (ultra-low-risk), 35% >2-5% (low-risk), 26% >5-10% (intermediate-risk) and 18% with >10-40% probability (intermediate-high risk) and 11 (3%) had ≥40% probability of progression at 2 years. The respective cumulative 2-year progression rate for these groups was 0%, 3%, 4%, 21% and 21% respectively ($p<0.001$). According to the Pangea 2.0 model without BM data, 25% had ≤2% probability (ultra-low) of progression at 2 years, 36% >2-5% (low-risk), 21% >5-10% (intermediate-risk), 18% >10-40% (intermediate-high risk) and just one patient ≥40% probability. The respective cumulative 2-year progression rate for these groups was 0%, 4%, 12%, 24% and 21% ($p<0.001$) (the single patient with >40% has not progressed). Overall, both Pangea models provided satisfactory discrimination (C-index: 0.765 and 0.798 for the model with and without BM data, respectively) and satisfactory explained variation (R2 0.091 and 0.092, respectively).
CONCLUSION: Both models successfully stratify patients with SMM according to their baseline risk, however, as static models they have mostly negative predictive value for progression, with low-risk patients having very low probability of imminent progression. Nonetheless, static models are insufficient for satisfactory risk prediction in intermediate or high-risk patients.

09. HIGH MRD NEGATIVITY RATE, LONG PFS, AND OPTIMIZED OCULAR MANAGEMENT IN INTERMEDIATE FIT AND FRAIL NEWLY DIAGNOSED MULTIPLE MYELOMA PATIENTS TREATED WITH BELAMAF, DARATUMUMAB, LENALIDOMIDE AND DEXAMETHASONE

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OBJECTIVE: Quadruplet regimens improved clinical outcomes, supporting belamaf + DRd evaluation in TI NDMM.

METHODS: BelaDRd, a phase 1/2, open-label study (EUCT-2021-006792-42) evaluated this combination in TI, intermediate-fit and frail, NDMM. Part 1 established belamaf 1.9 mg/kg Q8W, extended to Q12W as the recommended phase 2 dose (RP2D). Part 2 (dose-expansion phase) evaluates the safety and efficacy of the RP2D in two randomized cohorts, Groups A and B, where belamaf dosing was guided by ophthalmologist and hematologist decision (using Vision-Related Anamnestic, VRA tool), respectively.

RESULTS: At clinical cut off, 15th May 2026, in Part 1, 24 patients (pts) (median age: 73 years; male: 54.2%) entered the study; 12.5% had high-risk cytogenetics (HRC). At a median follow-up of 37.2 months, 18 (75%) pts were on treatment, and 6 (25%) discontinued; 4 (16.7%) death, 2 (8.3%) AE/SAE, 1 (4.2%) withdrew consent, and 1 (4.2%) due to progressive disease (PD). At baseline, 79.2% pts had cataract. Of 419 planned belamaf doses 111 (26.5%) were delayed/skipped due to OAEs. The median dose intensity (MDI) of belamaf was 0.5 mg/kg/Q4W. The overall ORR (≥ PR) was 91.7% (22/24). Sixteen pts (69.6%) achieved ≥CR (≥2 response assessments). MRD negativity was achieved in 14 (87.5%) of evaluable pts (n=16). In Part 2 (n=12; median age: 74 years; male: 58.3%); 16.7% of pts had HRC. At a median follow-up of 23.4 months, 11 pts (91.7%) remained on treatment; 1 pt (8.3%) discontinued due to PD. Overall 66.7% pts had cataract (Group A: 83.3%; Group B: 50%). Of 142 planned belamaf doses, 15 (10.6%) were skipped due to OAEs. Held doses as a proportion of planned doses was 16.7% (13/78) in Group A and 3.1% (2/64) in Group B. The MDI was 0.8 mg/kg/Q4W. The overall ORR was 91.7% (11/12). Eight patients (66.7%) achieved a response of ≥CR (Group A: 3 pts (50%); Group B:5 pts (83.3%)). MRD negativity was achieved in 6 (50%) of evaluable pts (n=8). The median time to ≥PR was 1.1 months for both parts. At 18 months, PFS rates were 91.7% (95% CI 76.4-97.2) overall and 87.5% (66.1-95.8) in the RP2D population; corresponding TTP rates were 97.1% (80.9-99.6) and 95.5% (71.9-99.4). Projected mPFS ranged from 104.8-190.8 months (8.7-15.9 years) overall and 89.5-195.0 months (7.4-16.2 years) in theRP2D population. Grade ≥3 BCVA decline was observed in 85 (10.5%) of ocular assessments in part 1 and 6 (4.3%) and 7 (5.8%) in part 2 groups A and B, respectively. Grade ≥3 OAEs without VRA-reported "substantial time" (>50% of the time) were detected in 1/58 (1.7%) of belamaf dosing cycle ophthalmologist assessments in Group B. Grade ≥2/≥3 keratopathy occurred in 12.7%/0.8% of assessments in Part 1; in Part 2, rates were 6.5%/0% (Group A) and 13.8%/0% (Group B). Median resolution time of ≥Grade 2 BCVA OAE/keratopathy was 1.1/1.0 months (Part 1) and 1.9/1.0 months (Part 2).

CONCLUSION: These findings support the continued development of BelaDRd as a promising frontline quadruplet regimen for NDMM, while reducing reliance on ophthalmologic examination.

10. VISION RELATED ANAMNESTIC (VRA) TOOL-GUIDED BELAMAF DOSING IN TRANSPLANT-INELIGIBLE PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA

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OBJECTIVE: The aim of this study was to evaluate safety, tolerability, and clinical activity of belamaf plus lenalidomide and dexamethasone (Rd) (BelaRd) in transplant ineligible newly diagnosed multiple myeloma (TI-NDMM) patients (pts).

METHODS: BelaRd trial (NCT04808037) was a phase 1/2, open label study in frail and intermediate-fit pts with NDMM. In Part 2, n=30 pts were treated at recommended part 2 dose (RP2D) of 1.9mg/kg and randomized 1:1. The study compared two strategies for managing ocular adverse events (OAEs). In Group A, belamaf dose modifications were guided by the Keratopathy and Visual Acuity (KVA) scale assessed by an opthalmologist. In Group B, dose modifications were based on patients' Vision-Related Anamnestic (VRA) questionnaire responses, which assessed ocular symptoms and their impact on activities of daily living (ADL); this questionnaire was evaluated by the treating hematologist. All patients of group B were also checked by an ophthalmologist and in case of the presence of ≥Grade 3 KVA events (reduced best-corrected visual acuity [BCVA] and/or corneal findings), the ophthalmologist decision was taken into account irrespective of the hematologist decision.

RESULTS: At the clinical data cut-off (15th May 2026), 19 of 30 patients (63.3%) in Part 2 were still receiving treatment. At baseline, ECOG PS was 1/2 in 56.7%/3.3%; R-ISS staging was II/III in 63.3%/10% and high-risk cytogenetics was present in 16.7% of pts. At baseline cataract was observed in 86.7% (26/30) pts; (14 (93.3%) in Gr A and 12 (80%) in Gr B). Overall response rate (ORR) (≥PR) was 96.7% in part 2 (sCR, 53.3%; CR, 3.3%; VGPR, 30%; and PR, 10%). Dose holds due to OAEs occurred in 22.7% of planned doses in Gr A (KVA) versus 2.7% in Gr B (VRA). Grade ≥3 OAEs without VRA-reported "substantial time" (>50% of total time) were detected in 7/354 (1.9%) (total number of assessments) and 2/168 (1.2%) (total number of dosing cycle) in Gr B. Grade ≥3 BCVA deterioration and keratopathy was observed in 7.6% (34/447) and 5.9% (21/354) of ophthalmologist assessments in Gr A and B, respectively. The median time to resolution of Grade ≥2 keratopathy and BCVA ocular events was 1.8 months (range 0.9-14.9) in Gr A and 1.2 months (range 0.9-3.7) in Gr B. In part 2 overall, the absence of patient reported blurry or poor vision on the VRA was associated with low frequency of Grade ≥2 keratopathy (6/351 (1.7%) and 2/243 (0.8%) of assessments, respectively and no grade ≥3 Keratopathy was observed among patients reporting no blurry or poor vision on the VRA. The absence of patient reported blurry or poor vision on the VRA Grade ≥2 BCVA was 33/351 (9.4%) and 19/243 (7.8%) of assessments and Grade ≥3 was 1/351 (0.2%) and none, respectively. Driving/reading discontinuation due to eyesight issues occurred in 0.5%/0.6% of monthly assessments in Gr B and 0.0%/0.2%in Gr A.

CONCLUSION: These findings support further evaluation of the VRA as a dosing-guidance tool and suggest that its use may reduce or potentially eliminate the need for routine pre-dose ophthalmic examinations in patients receiving belamaf.

11. IMPACT OF MRD IN THE OUTCOME OF PATIENTS WITH LIGHT CHAIN (AL) AMYLOIDOSIS TREATED UPFRONT WITH DARATUMUMAB

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OBJECTIVE: In AL amyloidosis, undetectable minimal residual disease (MRD) has been associated with lower probability of hematologic relapse and higher probability of organ responses, but its role in the daratumumab era has not been validated.

METHODS: In order to evaluate the prognostic role of MRD, we analyzed the data of 87 patients who have received upfront daratumumab, had achieved hemCR or hemVGPR and were evaluated for MRD using next generation flow cytometry (NGF), at 6 and/or 12 months.

RESULTS: At diagnosis, 44% were female and median age was 62 years. Distribution per Mayo stage 1, 2, 3a and 3b was 15%, 46%, 22% and 17%, respectively; 59% had renal and 80.5% cardiac involvement. The hematologic response at the time of MRD was hemCR in 68 and hemVGPR in 19 patients. Among hemCR patients, 60 (88%) had lambda and 8 (12%) kappa isotype; among hemVGPR 11 (58%) had lambda and 8 (42%) kappa, respectively. At 6- and 12-month landmarks, 75/87 and 82/87 patients were assessed for MRD; 27/75 (31%) and 29/82 (33%) were MRD negative (MRDneg); none of hemVGPR patients achieved MRD negativity. Among 43 patients that were tested as MRDpos at 6 months, only one converted to MRDneg, while among 29 that were tested as MRDneg at 6 months, 2 converted MRDpos at 12 months, both at the level of detection (10-6). MRDneg patients at either the 6- or 12- month landmark, had more frequent renal involvement (74% vs 50% for MRDpos, p=0.040). Notably, lambda patients achieved higher rates of MRD negativity; 42% were MRDneg vs only 6% of kappa, p=0.008), and this remained significant when we focused the analysis on patients with hemCR (50% of lambda were MRDneg vs 12.5% of kappa [p=0.046]). At 6-month landmark, cardiac response was observed in 64% of MRDneg vs 68% of MRDpos patients (p=0.772) and at 12-month landmark in 76% vs 77% (p=0.783), respectively. At 6-month landmark renal response was observed in 57% of MRDneg vs 43% of MRDpos (p=0.371), and at 12-month landmark (n=44), in 58% vs 56.5% (p=0.569), respectively. Median follow-up was 41 months; 4-year OS was 93% and there was no significant difference according to MRD status. At 6-month landmark, 4-year event free survival (EFS) rate for MRDneg was 100% vs 77% of MRDpos (p=0.038) and among patients with hemCR was 100% vs 85% (p=0.299). At 12-month, 4-year EFS rate for MRDneg was 100% vs 78% (p=0.029) and among patients with hemCR, 100% vs 86% (p=0.072). Among those MRDneg at 12-month landmark, none of the 29 patients required further treatment vs 12/56 MRDpos (p=0.023), and among hemCR patients, 0/29 vs 5/31 had relapsed from CR (p=0.060), respectively.

CONCLUSION: The attainment of early and sustained MRD negativity is associated with prolonged OS and very low probability of requiring further treatment, among AL amyloidosis patients treated with upfront daratumumab. Interestingly, patients with kappa isotype achieved less frequently MRD negativity, which highlight that this subgroup may have distinct clinical and biological features. Notably, continuing treatment beyond 6 months did not seem to improve MRD negativity rates.

12. INCIDENCE OF INFECTION IN LYMPHOMA PATIENTS UNDERGOING ALLOGENEIC STEM CELL TRANSPLANTATION

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OBJECTIVE: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the only potentially curative treatment option for many types of lymphoma. Infection is one of the most serious and frequent complications of allo-HSCT. This study aimed to determine the frequency of infection in lymphoma patients undergoing allo-HSCT, identify the causative agents of infection, and evaluate the impact of infection on transplant outcomes.

METHODS: This study retrospectively reviewed data from 58 patients who underwent allo-HSCT with a diagnosis of lymphoma at our transplant clinic between 2012 and 2024. The study examined the patients' dermatographic characteristics, transplant-related clinical data, infection history before, during, and within three months after discharge, the identified infectious agent, and the effects of these infections on transplant outcomes.

RESULTS: The study included a total of 58 patients, 20 (34.5%) women and 38 (65.5%) men, with a median age of 49 years (22-70 years). Eighteen patients (31%) experienced infections in the pre-transplant period. Of the 58 patients, 46 (79.3%) used GCSF. All patients received antiviral prophylaxis before transplantation. Three patients (5.2%) did not receive prophylaxis against bacterial or fungal agents. During transplantation, 27 (46.6%) patients had viral infections, 19 (32.8%) had bacterial infections, and 9 (15.5%) had fungal infections. The most frequently observed viral infection was CMV infection (n:28, 48.3%), while the most commonly cultured bacterial infections were Staphylococcus aureus (n:5, 8.6%) and E. coli (n:4, 6.9%). Neutropenic fever was observed in 35 patients (60.3%) during transplantation. Thirty-nine patients (67.2%) had CRP levels above 100. The highest median CRP value during transplantation was 141.5 (2.8-489). The median length of hospital stay was 37.5 (6-81) days. Overall survival (OS) was lower in patients with neutropenic fever (58.8(18.7-1523) months) compared to those without (68.6 (13-1457) months). Viral infection was more frequent (n:12, 63.2%) in patients who received ATG. The OS of the patients was 60.8 (13-1523) months. 41 (70.7%) of the patients participating in the study died. The total number of deaths due to infection was 26 (44.8%). Nineteen patients (32.8%) died due to infection within 3 months of transplantation. Of the patients who died, 13 (31.7%) had bacterial infections, 18 (43.9%) had viral infections, and 6 (14.6%) had fungal infections. Multiple microorganisms were present in 5 patients (31.3%). The OS of patients who died due to infection was lower than that of those who did not (median (min-max) 53(13-1457) months - 68 (13-1523) months).

CONCLUSION: There are studies in the literature regarding the frequency of infections in patients after autologous or allogeneic stem cell transplantation (1,2,3). However, the number of studies on the frequency of infections after allo-HSCT in lymphoma patients is quite limited. In our study, it was seen that viral infections were the most frequent. The total number of patients who died due to infection was 26 (44.8%). Patients who died due to infection during the transplant process had a lower OS rate than those who did not. More comprehensive studies are needed on measures to reduce the incidence of infection, one of the most important parameters affecting transplant outcomes and survival in patients undergoing allo-HSCT.

POSTER PRESENTATIONS

P01. PRIMARY CUTANEOUS FOLLICLE CENTER LYMPHOMA PRESENTING AS AN ULCERATIVE LESION OF THE NASAL ALA: A CASE REPORT

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OBJECTIVE: Primary cutaneous B-cell lymphomas (PCBCLs) are a heterogeneous group of extranodal non-Hodgkin lymphomas confined to the skin at diagnosis, accounting for approximately 25% of all primary cutaneous lymphomas. According to the WHO-EORTC classification and the 2022 International Consensus Classification (ICC), they comprise several distinct clinicopathological entities. Primary cutaneous follicle center lymphoma (PCFCL) is an indolent subtype that is typically limited to the skin and can be effectively managed with local treatment. However, distinguishing PCFCL from systemic follicular lymphoma with secondary cutaneous involvement (sFL-CI) remains a diagnostic challenge because of their overlapping clinical, histopathological, and immunophenotypic features, with important implications for staging, prognosis, and treatment.

METHODS: Clinical presentation, histopathological findings, staging procedures, and management of a patient with primary cutaneous follicle center lymphoma were retrospectively reviewed.

RESULTS: A 62-year-old man with a history of well-controlled hypertension presented with a non-healing ulcerative lesion on the right nasal ala. He had no B symptoms, and complete blood count and routine biochemical parameters were within normal limits. An excisional biopsy was performed with a preliminary diagnosis of basal cell carcinoma. Histopathological examination revealed a lymphoid infiltrate composed of medium-sized atypical cells with vesicular and indented nuclei, some containing prominent nucleoli. Immunohistochemistry demonstrated positivity for LCA, CD20, BCL2, and BCL6, while CD10, MUM1, and CD30 were negative. The Ki-67 proliferation index was approximately 10-15%. The pathological findings were consistent with either primary cutaneous follicle center lymphoma (PCFCL) or secondary cutaneous involvement by systemic follicular lymphoma. Histopathological evaluation confirmed negative surgical margins. Comprehensive staging was performed to exclude systemic disease. Fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) demonstrated no evidence of systemic lymphoma involvement. Bone marrow aspiration showed no lymphomatous infiltration, while the bone marrow biopsy result is pending. The patient was scheduled for multidisciplinary discussion involving hematology, pathology, radiation oncology, and nuclear medicine to determine the optimal post-excisional management, including involved-site radiotherapy versus close clinical observation, following completion of the staging work-up.

CONCLUSION: In our patient, BCL2 positivity initially raised suspicion for secondary cutaneous involvement by systemic follicular lymphoma. Nevertheless, FDG PET/CT and bone marrow aspiration showed no evidence of systemic disease. Although PCFCL typically lacks BCL2 expression, BCL2 positivity has been reported in approximately 10-40% of cases, limiting its specificity for systemic follicular lymphoma. Therefore, BCL2 expression should always be interpreted in conjunction with the clinical presentation, comprehensive staging, and additional pathological findings. To further investigate the possibility of an underlying IGH: BCL2 rearrangement, fluorescence in situ hybridization (FISH) analysis was requested on the bone marrow biopsy specimen, and the result is currently pending. This case highlights the importance of a multidisciplinary diagnostic approach integrating histopathology, immunophenotyping, molecular studies, and systemic staging to establish the correct diagnosis and guide appropriate management.

P02. THE PREDICTIVE VALUE OF MUSCLE MASS AND ADIPOSITY INDICES IN OVERALL SURVIVAL OF NEWLY DIAGNOSED PATIENTS WITH MULTIPLE MYELOMA

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OBJECTIVE: Body composition has been found to be associated with both the risk of developing solid and hematological malignancies and disease outcomes. However, the evidence regarding the role of body composition in disease outcomes in multiple myeloma (MM) remains limited. Therefore, this study aimed to explore the prognostic value of body composition indices in survival of patients with newly diagnosed MM (NDMM).
METHODS: A total sample of 200 consecutive patients with NDMM, who treated at a single center, were included in this study. All patients undergone baseline low-dose whole body computed tomography (WBCT) as part of their clinical routine and before first-line treatment initiation. From WBCT, images at the L3 vertebra were extracted manually and analyzed using an artificial intelligence-driven software Quantib Body Composition software (Quantib Body Composition, version 0.2.1, DeepHealth, Rotterdam, the Netherlands). From tissue segmentation, the software reports the cross-sectional area of the subcutaneous and visceral fat, and psoas, abdominal and long spine muscles. Subsequently, the height-corrected indices were calculated, including the skeletal muscle index (SMI), subcutaneous adipose tissue index (SATI), and visceral adipose tissue index (VATI). The sex-specific tertiles of these indices were used for analysis, using first tertile as the reference category. As an addition index of splanchnic adiposity, liver attenuation was measured using a standardized multi-segment ROI approach and the sex-specific tertiles were also used in the analysis. The primary outcomes of the study were the progression-free survival (PFS) and overall survival (OS). Simple and multiple (adjusted for age, sex, performance status, R-ISS and autologous stem cell transplantation (ASCT) Cox regression models were performed to examine the association between body composition indices and PFS or OS.
RESULTS: Multivariate Cox regression analysis showed that patients with higher SMI (third tertile) had significantly lower risk of mortality than those at the first tertile (HR:0.40, 95%CI:0.19-0.86, p=0.019). Neither SATI nor VATI were found to associate with PFS or OS (p> 0.05), but a significant increased risk of mortality was found with higher SATI values (examined as continuous variable) when SMI was added to the adjusted model (HR:1.01, 95%CI:1.00-1.02, p=0.005). In addition, the analysis revealed that patients in the middle and higher tertiles of liver attenuation had significantly lower mortality risk compared with those in the lowest tertile (HR:0.41, 95%CI:0.22-0.75, p=0.004; HR:0.53, 95%CI:0.29-0.94, p=0.030, respectively). Subgroup analysis among non-ASCT patients confirmed the those at the higher SMI tertile had significantly lower risk of mortality than those at the lowest tertile (HR: 0.43, 95%CI: 0.19 - 0.97, p= 0.041).
CONCLUSION: These results confirm the predictive and clinical value of body composition in disease outcomes among patients with NDMM, where higher skeletal mass and lower splanchnic adiposity seem to predict survival. The body composition indices examined in this study were estimated from routinely performed WBCT, which supports their clinical usefulness in risk stratification.

P03. A SYSTEMATIC REVIEW AND META-ANALYSIS OF COMPLEMENT INHIBITION FOR TRANSPLANT-ASSOCIATED THROMBOTIC MICROANGIOPATHY

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OBJECTIVE: Transplant-associated thrombotic microangiopathy (TA-TMA) is a life-threatening endothelial injury syndrome following hematopoietic cell transplantation. Recently, narsoplimab has become the first United States Food and Drug Administration-approved therapy for TA-TMA. Nevertheless, evidence for complement-directed therapy remains fragmented, and previously published meta-analyses have focused only on eculizumab. Therefore, the objective of this systematic review and meta-analysis is to evaluate the efficacy and safety of complement inhibition in adult and pediatric TA-TMA.

METHODS: MEDLINE, Scopus, the Cochrane Library, American Society of Hematology and European Hematology Association conference abstracts, and clinical trial registries were searched through April 2026. Interventional and observational studies, including those with a single-arm design, evaluating complement inhibitors in both adult and pediatric TA-TMA were eligible. Primary outcomes included overall response rate (ORR), complete response rate (CRR), and survival rate (SR), while safety outcomes were considered adverse events and cause-specific mortality. Random-effects meta-analyses of proportions were performed in R, with prespecified subgroup analyses by complement inhibitor, age group, and study design. Moreover, risk of bias was assessed using design-appropriate validated tools.

RESULTS: Nineteen studies (3 clinical trials and 16 observational studies), comprising 342 patients, were included. Across all complement inhibitors, pooled ORR was 65% (95% confidence interval [CI], 60-71%; I^2=0%), CRR 41% (95% CI, 31-52%; I^2=60.9%), and SR 51% (95% CI, 41-61%; I^2=62.7%). Pooled ORR was 73% (95% CI, 58-86%) with ravulizumab, 64% (95% CI, 58-71%) with eculizumab, and 63% (95% CI, 48-76%) with narsoplimab; corresponding CRRs were 31% (95% CI, 0-75%), 45% (95% CI, 34-55%), and 42% (95% CI, 18-68%), respectively. Differences between complement inhibitors were not significant for ORR or CRR (p=0.539 and p=0.838). Additionally, pooled SR was 89% (95% CI, 77-98%) with ravulizumab, 47% (95% CI, 39-55%) with eculizumab, and 46% (95% CI, 29-64%) with narsoplimab, with a significant subgroup difference (p<0.0001). Adult patients had a numerically higher ORR than pediatric patients (69% vs 64%), whereas pediatric patients had numerically higher CRR (50% vs 34%) and SR (61% vs 40%). However, none of these differences reached statistical significance. Clinical trials showed numerically higher ORR (67% vs 64%) and SR (66% vs 48%), whereas observational studies yielded a higher CRR (44% vs 36%); differences by study design were not significant. According to safety outcomes, reported treatment-emergent adverse events were predominantly bacterial, viral, and fungal infections, with occasional skin reactions. Infections were the leading cause of death (29%; 95% CI, 16-43%), followed by TA-TMA (18%; 95% CI, 4-36%), other or unknown causes (11%; 95% CI, 1-26%), graft-versus-host disease (5%; 95% CI, 0-15%), and relapse (3%; 95% CI, 0-11%).

CONCLUSION: Complement inhibition is associated with clinically meaningful responses and survival outcomes in TA-TMA and appears to be generally well tolerated. Nevertheless, our findings are limited by predominantly observational evidence, substantial heterogeneity, and between-study differences in patient selection and outcome definitions. Prospective, multicenter studies using standardized endpoints are needed.

P04. VENETOCLAX-ASSOCIATED CARDIOVASCULAR TOXICITY IN ACUTE MYELOID LEUKEMIA: AN UNDERESTIMATED THREAT?

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OBJECTIVE: Venetoclax, a selective B-cell lymphoma 2 (BCL-2) inhibitor, in combination with azacitidine, consists the cornerstone of treatment for older patients with newly diagnosed acute myeloid leukemia (AML) who are not eligible for intensive chemotherapy. Although generally well tolerated, emerging evidence suggests a potential association between venetoclax and cardiovascular toxicity, particularly during the early phase of treatment.
METHODS: We report a case of severe, potentially fatal, cardiotoxicity occurring shortly after initiation of venetoclax and azacitidine therapy.
RESULTS: A 71-year-old woman with a history of hypothyroidism was newly diagnosed with intermediate-risk AML. Treatment with azacitidine and venetoclax was initiated. On day 7 of therapy, she developed ventricular fibrillation, without chest pain, followed by cardiac arrest, requiring immediate resuscitation, endotracheal intubation, and transfer to the coronary intensive care unit (ICU). Prolongation of the QTc interval (530msec) was observed, which had not been present on the initial electrocardiogram. Neither electrolyte abnormalities, nor other pharmacological agents were identified as causative factors during evaluation. Echocardiographic assessment demonstrated a marked reduction in left ventricular systolic function, with an ejection fraction below 30% and diffuse hypokinesia. Notably, the pre-treatment echocardiogram was normal. Coronary angiography was considered; however, the patient's family declined the procedure. Therefore, obstructive coronary artery disease could not be definitively excluded. However, troponin serum levels remained stable, making the diagnosis of an acute ischemic event less likely. An external temporary pacemaker was placed and pharmacological treatment for heart failure per ICU protocol was initiated. The patient's clinical course was complicated by severe hemodynamic instability, followed by acute hepatic dysfunction and both upper- and lower-limb ischemia. Venetoclax was considered the most likely cause of the acute cardiac dysfunction, given its temporal association with treatment initiation and the lack of another precipitating factor being identified. Bone marrow reassessment at the end of the first cycle showed complete remission. Nevertheless, the patient's overall clinical condition deteriorated, and she ultimately died in the ICU from septic shock complicated by lower-extremity gangrene.
CONCLUSION: Although cardiovascular adverse events associated with venetoclax are considered uncommon, accumulating reports suggest that clinically significant cardiotoxicity, comparable to that of anthracyclines (OnueT et al. Cardiooncology2024), may occur. Proposed mechanisms include modulation of oxidative stress, cardiac inflammation, and apoptosis through pathways involving nuclear factor kappa B (NF-κB) and BCL-2 signaling (AlAsmari AF et al. Int J Mol Sci.2022). However, the available evidence remains limited, and no evidence-based recommendations currently exist for the prevention, monitoring, and management of venetoclax-associated cardiotoxicity. This case highlights the importance of maintaining a high index of suspicion for acute cardiovascular complications in older patients receiving venetoclax-based therapy for AML. Early recognition of new cardiac symptoms, prompt assessment of cardiac function and biomarkers, and close collaboration between hematology, cardiology, and intensive care teams may facilitate timely intervention. Baseline cardiovascular assessment and close cardiac monitoring during the early phase of treatment should be considered, particularly in patients of advanced age and/or with cardiovascular risk factors. Further prospective studies are warranted to better characterize the incidence, risk factors, and optimal management strategies for venetoclax-associated cardiotoxicity.

P05. A RARE TRANSLOCATION IN ACUTE MYELOID LEUKEMIA WITH A BZIP IN-FRAME CEBPA MUTATION

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OBJECTIVE: To describe a case of acute myeloid leukemia (AML) harboring the uncommon chromosomal translocation t(2;20)(q13;p13) in association with a bZIP in-frame CEBPA mutation. Given the limited data regarding the occurrence and prognostic significance of t(2;20)(q13;p13), this case aims to contribute to the existing literature and to explore its potential relationship with CEBPA-mutated AML and treatment response.

METHODS: A 62-year-old male with a medical history of severe bicuspid aortic valve stenosis that was recently diagnosed, was referred to our emergency department due to leukocytocis, anemia and thrombocytopenia, identified during preoperative evaluation for aortic valve replacement. On admission, the patient had a white blood cell count of 17.670/mL, a hemoglobin 11.4g/dL and a platelet count of 79.000/mL. A bone marrow aspiration revealed hypercellularity, infiltration of 57% by blasts of medium to large size, some with granules and Auer rods, markedly depressed granulocytic lineage, with a maturation block, eosinophils, rich erythroid lineage with dyserythropoietic changes and few megakaryocytes. Immunophenotypic analysis using flow cytometry highlighted a prominent blast population of 60% expressing MPO(+), HLADR(+), CD13(-), CD33(+)weak, CD34(+), CD38(+), CD7(+)weak, CD117(+), CD123(-).

RESULTS: The patient was assessed by the hospital's cardiologist team and was scheduled for transcatheter aortic valve implantation. Until then and due to the severe aortic stenosis the patient received less intensive therapy with hypomethylating agent azacitidine and BCL2-inhibitor venetoclax. After the first cycle patient achieved complete remission. In the meantime, the NGS results were obtained and revealed a bZIP in-frame CEBPA mutation, with no detection of germline mutations. According to the ELN 2022 criteria the patient was classified into the favorable risk category. Conventional cytogenetic analysis demonstrated 46,XY,t(2;20)(q13;p13), with the translocation present in all 20 metaphases analyzed. A focused literature search identified a previously published AML case carrying t(2;20)(q21;q13.1), but not the same breakpoint combination. Patient underwent transcatheter aortic valve implantation and he was then able to receive induction therapy according to "7+3" protocol (Cytarabine+Idarubicin), after which achieved complete remission. The patient continued with "2+5" (Cytarabine+Idarubicin). He is currently on consolidation therapy with IDAC.

CONCLUSION: The present case describes a rare t(2;20)(q13;p13) in AML detected in all metaphases analyzed in association with a bZIP in-frame CEBPA mutation. Although CEBPA mutated AML represents a genetically defined AML entity, the concomitant cytogenetic abnormality t(2;20)(q13;p13) has not been established as a recurrent genetic lesion in AML or any other hematologic malignancy. Its coexistence with a CEBPA mutation raises the possibility of a previously unrecognized association; however, the biological and prognostic significance of t(2;20)(q13;p13) remains uncertain and there is no evidence that it modifies the favorable prognostic significance of CEBPA-mutated AML. Further molecular characterization of the 2q13 and 20p13 breakpoints will be valuable to determine whether the rearrangement generates a pathogenic fusion or disrupts regulatory elements. Additional cases will be required to establish whether this represents a recurrent biological association or an incidental cytogenetic event.

P06. FROM CYTOPENIAS AND SYNDROMIC FEATURES IN CHILDHOOD TO MDS: UNMASKING A POSSIBLE EMBERGER SYNDROME

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OBJECTIVE: GATA2 deficiency is a well-established predisposing factor for myeloid neoplasms, including acute myeloid leukemia (AML), myelodysplastic neoplasms (MDS), and chronic myelomonocytic leukemia, with disease evolution frequently associated with monosomy 7, trisomy 8, and acquired somatic mutations in ASXL1 or STAG2. GATA2 is a master transcription factor crucial for the proliferation and survival of hematopoietic stem cells, and its deficiency is associated with a heterogeneous clinical spectrum encompassing myeloid neoplasms, immunodeficiency, and syndromic manifestations. Disease onset is highly variable, with many patients being diagnosed in the setting of an established myeloid neoplasm. To date, more than 150 mutations have been described. We report a case of MDS in a 27-year-old patient with longstanding cytopenias, congenital and extra-hematological abnormalities, harboring a GATA2 variant highly suggestive of germline origin, highlighting the importance of considering inherited predisposition syndromes in young patients with otherwise unexplained cytopenias, especially in addition to syndromic features.
METHODS: We retrospectively reviewed the patient's clinical presentation, laboratory findings, serial bone marrow evaluations, cytogenetic and molecular analyses, including whole-exome sequencing (WES) and targeted myeloid next-generation sequencing (NGS), treatment, and clinical course.
RESULTS: A 27-year-old patient with a history of surgically corrected tetralogy of Fallot at the age of 4, resected hepatic adenoma, and hearing impairment was referred in 2025 for evaluation of progressive cytopenias. Family history is unavailable, as he is adopted. Upon referral, CBC demonstrated anemia (Hb 9.4g/dL) and neutropenia (WBC 3.27x109/L; ANC 1.27x109/L), with a preserved platelet count of 207x109/L. Neutropenia had been documented since childhood, but the initial diagnostic work-up was inconclusive, as the laboratory findings were not correlated with the patient's clinical features. In 2023, he was hospitalized with pancytopenia, and bone marrow evaluation demonstrated hypocellularity, with a normal male karyotype, but a definitive diagnosis was again not reached. Given the early onset and persistence of cytopenias, genetic evaluation was pursued. WES of peripheral-blood identified a heterozygous pathogenic nonsense variant in GATA2, NM_032638.5:c1084G>A, p.(Arg362*), predicted to result in loss of protein function. Due to the sample type, a germline origin could not be definitively established. During follow up, cytopenias progressively worsened. Bone marrow evaluation demonstrated dysplastic changes suggestive of MDS with increased blasts (MDS-IB1), while conventional cytogenetics showed again a normal male karyotype. Myeloid NGS detected the GATA2 variant at a VAF of 49.25%, along with three additional STAG2 mutations. According to the IPSS-M, the patient was classified as high risk. Additionally, given his young age, longstanding cytopenias, pathogenic GATA2 variant and subsequent development of MDS, evaluation for allo-HSCT was initiated. A VAF approaching 50% further raised suspicion of a germline origin; additional confirmatory testing in non-hematopoietic tissue is planned.
CONCLUSION: The presented case highlights the importance of investigating underlying germline predisposition in young adults with longstanding cytopenias and congenital or extra-hematological anomalies, indicative of a bone marrow failure syndrome. Recognition of a GATA2-associated disorder before progression to an overt myeloid neoplasm is crucial for genetic counseling, donor selection, surveillance, and timely therapeutic planning, including consideration for allogeneic transplantation.

P07. T(11;14)(Q13;Q32) WITHOUT CCND1: IGH REARRANGEMENT IN ACUTE MYELOID LEUKEMIA: A WELL-KNOWN TRANSLOCATION IN AN UNEXPECTED DISEASE

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OBJECTIVE: The t(11;14)(q13;q32), involving rearrangement of the CCND1 and IGH loci, is a characteristic cytogenetic finding in mantle cell lymphoma and is also found in other lymphoproliferative disorders and multiple myeloma. We present an extremely rare case of Acute Myeloid Leukemia (AML), in which conventional cytogenetic analysis revealed a t(11;14)(q13;q32), while FISH analysis showed no CCND1::IGH rearrangement.
METHODS: We reviewed the patient's clinical course, Bone Marrow (BM) evaluation, cytogenetic analysis, and treatment, along with a literature review reporting the rare genetic finding.
RESULTS: In May 2026, a 74-year-old female with unremarkable past medical history was incidentally found to have abnormal complete blood count and was referred for further evaluation. BM aspiration showed 60% blast infiltration along with trilineage dysplasia, while BM-immunophenotype and biopsy confirmed the diagnosis of Acute Myelomonocytic Leukemia. Twenty metaphases were analyzed in the BM sample, revealing an abnormal clone with the karyotype:46,XX,t(11;14)(q13;q32),?inv(21)(p13q22.1), while targeted myeloid NGS demonstrated a SRSF2 mutation(VAF 48,2%). An AML-Myelodysplasia Related diagnosis, according to WHO 2022, was established and the disease was further classified as favorable risk according to ELN 2024. Treatment with Azacitidine+Venetoclax (AZA-VEN) was initiated. On day 50, BM evaluation showed refractory disease, while an extramedullary myeloid focal lesion in the right hand was identified. The diagnosis was confirmed by biopsy as myeloid sarcoma. The patient is currently receiving salvage therapy with AZA-VEN plus selinexor, along with localized radiotherapy for the extramedullary lesion. Since t(11;14)(q13;q32), is a well-known rearrangement related to lymphoid, but not myeloid malignancies, we further tested the neoplastic cells in order to exclude the possibility of double neoplasm infiltration. FISH analysis of 100 interphase nuclei showed a normal 2G:2O hybridization pattern, with two green signals corresponding to IGH (14q32.33) and two orange signals corresponding to CCND1 (11q13.3), with no evidence of CCND1::IGH rearrangement. Metaphase FISH demonstrated one IGH signal on the normal chromosome 14 and one CCND1 signal on the normal chromosome 11, whereas the second IGH signal was located on der(11) and the second CCND1 signal on der(14), without fusion signals. These findings indicate that the breakpoints of the t(11;14) lie outside the genomic regions covered by the specific CCND1 and IGH probe targets.
CONCLUSION: This case demonstrates that a cytogenetically apparent t(11;14)(q13;q32) does not necessarily represent the classical CCND1::IGH rearrangement. Metaphase FISH was crucial for characterizing the rearrangement and distinguishing it from the canonical t(11;14)/CCND1::IGH associated with B-cell lymphoid neoplasms, emphasizing the complementary role of the two methods in the investigation of hematological malignancies, particularly when apparently discordant findings are obtained by the two methods. A review of the literature identified only one previously reported case of this exceptionally rare cytogenetic rearrangement in AML (Tarsitano M. et al. 2009). Although the limited number of reported cases cannot establish a definite correlation between the cytogenetic findings and the clinical features (ie monocytic component) or prognosis (resistance to first-line therapy), the translocation warrants further investigation. Additional cases, with comprehensive clinical and molecular characterization, are required to clarify the potential biological and clinical significance of this unusual rearrangement.

P08. SECONDARY MALIGNANCIES IN CML: INCREASED RISK AND AT YOUNGER AGE - EFFECT OR COINCIDENCE?

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OBJECTIVE: Tyrosine kinase inhibitors (TKIs) have substantially improved survival in patients with chronic myeloid leukemia (CML), increasing interest in long-term complications, including secondary malignancies (sM). Prior studies have reported conflicting estimates of secondary malignancy risk and have not consistently demonstrated associations with specific TKIs or disease-intrinsic factors. We evaluated the incidence of secondary malignancies and their associations with ever-exposure to imatinib, nilotinib, and dasatinib, molecular response, clinical risk factors, and additional clonal abnormalities.

METHODS: We conducted a multicenter retrospective cohort study of patients with CML treated at eight centers in Greece. Patients with incomplete sM data were excluded, yielding 172/211 evaluable patients. Associations of sM with ever-exposure to imatinib, nilotinib, and dasatinib, time to major molecular response (MMR), time to deep molecular response (dMR), smoking, alcohol use, family history of cancer, body mass index (BMI), and additional clonal abnormalities at diagnosis were assessed. Statistical associations were evaluated using chi-square and Fisher's exact tests, independent t-tests, and multivariate logistic regression adjusted for age at CML diagnosis.

RESULTS: Among 172 patients, 54 (31.4%) developed an sM during a median follow-up of 10.7 years. sM rates were not significantly associated with smoking (P=1.000), alcohol use (P=1.000), family history of cancer (P=0.152), or BMI (P=1.000). Ever-exposure to imatinib was associated with sM in 37/121 patients (30.6%), compared with 17/51 (33.3%) unexposed patients (P=0.723). Nilotinib exposure was associated with sM in 16/57 patients (28.1%) versus 38/115 (33.0%) unexposed patients (P=0.601). Dasatinib exposure was associated with sM in 6/32 patients (18.8%) versus 48/140 (34.3%) unexposed patients (P=0.096). No exposure group difference was statistically significant. Molecular response depth (P=0.354) and time to MMR (P=0.292) or dMR (P=0.560) were not significantly associated with sM development. In age-adjusted multivariate logistic regression, dasatinib exposure showed a trend toward lower odds of sM (OR=0.34, 95% CI, 0.11-1.01; P=0.052), but this did not reach statistical significance. Major route abnormalities at diagnosis were associated with sM development: 5/10 patients (50.0%) with abnormalities developed sM, compared with 12/116 (10.3%) without abnormalities (P=0.0041). After adjustment for age and TKI exposure, they remained an independent predictor (OR=8.05, 95% CI, 1.9-34.1; P=0.005), corresponding to eightfold higher odds. Several sMs occurred at younger ages than population medians: bladder cancer (52.8 vs. 73 years), breast cancer (47.5 vs. 62 years), and endometrial cancer (46.4 vs. 63 years).

P08. (continue)

CONCLUSION: The observed cumulative incidence of secondary malignancies in this cohort (31.4%) appeared higher than the estimated annual cancer incidence in the general population (approximately 0.4%-0.6%, depending on age). This excess may reflect prolonged survival, follow-up, surveillance intensity, differences in ascertainment, confounding, and methodological factors, including malignancies diagnosed within the first year after CML diagnosis. Disease-related genomic instability and TKI-mediated effects on immune regulation or off-target kinase pathways are biologically plausible but remain unproven. Additional clonal abnormalities at diagnosis independently predicted sM, whereas TKI exposure was not significantly associated with risk. Because TKI exposure can change over time, studies should use time-varying exposure and competing-risk methods to account for switching, duration, and death before sM.

P09. RAPID MOLECULAR RESPONSES WITH 2G TKIS BUT COMPARABLE SURVIVAL: REAL-WORLD OUTCOMES OF FRONTLINE TKI SELECTION IN CML

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OBJECTIVE: Chronic myeloid leukemia (CML) is characterized by the BCR::ABL1 fusion gene and is treated predominantly with tyrosine kinase inhibitors (TKIs). Imatinib remains an effective first-line treatment; however, second-generation TKIs (2G TKIs) may induce more rapid and deeper molecular responses. The impact of frontline TKI on the requirement for treatment modifications, achievement of major molecular response (MMR), deep molecular response (dMR), treatment-free remission (TFR), and survival remains questionable. This study compared molecular response kinetics, treatment requirements, TFR outcomes, and overall survival (OS) between patients receiving frontline imatinib and those receiving frontline 2G TKIs.

METHODS: We conducted a comparative analysis of 184 patients with CML, including 83 initially treated with imatinib and 32 with 2G TKIs. The primary outcomes were MMR achievement and time to MMR. Secondary outcomes included the rate and time to dMR, treatment changes required to achieve MMR and dMR, TFR attempts and success among patients who achieved dMR, TFR duration, and OS. The number of patients included in each analysis varied according to the availability of outcome-specific data. Continuous variables were compared using independent-samples t-tests, whereas categorical variables were assessed using chi-square or Fisher's exact tests, as appropriate. Statistical significance was defined as $P<0.05$.

RESULTS: MMR was achieved in 78 of 82 patients (95.1%) receiving imatinib and 27 of 32 patients (84.4%) receiving a 2G TKI; this difference was not statistically significant (P=0.114). However, patients receiving 2G TKIs achieved MMR significantly faster than those receiving imatinib, with mean times of 9.0±7.0 and 18.2±18.9 months, respectively ($P<0.001$). dMR was achieved in 70 of 79 patients (88.6%) in the imatinib group and 25 of 31 patients (80.6%) in the 2G TKI group, with no statistically significant difference (P=0.354). Nevertheless, the mean time to dMR was significantly shorter among patients receiving 2G TKIs than among those receiving imatinib, at 21.4±22.8 versus 40.3±48.1 months (P=0.017). Patients treated with imatinib underwent more treatment changes than those treated with 2G TKIs, although the difference did not reach statistical significance (0.48±0.84 vs 0.29±0.50 changes; P=0.067). TFR was attempted by 27 of 81 patients (33.3%) in the imatinib group and 13 of 32 patients (40.6%) in the 2G TKI group; this difference was not statistically significant (P=0.516). Mean TFR duration was comparable between groups (38.6±39.3 vs 41.7±32.8 months; P=0.874). OS was also comparable (94.0% for imatinib vs 100.0% for 2G TKIs; P=0.321), with similar mean survival durations of 136.1±92.9 and 104.1±131.1 months, respectively (P=0.196).

P09. (continue)

CONCLUSION: Frontline 2G TKIs were associated with significantly faster achievement of MMR and dMR than imatinib, as well as fewer treatment changes, although the difference in treatment changes was not statistically significant. No significant differences were observed in overall MMR or dMR achievement rates. Among patients who achieved dMR and attempted TFR, TFR success and duration did not differ significantly between groups. OS was likewise comparable. These findings suggest that frontline 2G TKIs may accelerate molecular response, whereas TFR and survival outcomes may be shaped by subsequent disease management and patient-related factors. These findings are consistent with evidence from randomized trials.

P10. SERUM OPG AND RANKL LEVELS IN MYELOPROLIFERATIVE NEOPLASMS: A DISTINCTIVE PROFILE IN MYELOFIBROSIS

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OBJECTIVE: Alterations of the bone marrow microenvironment are a hallmark of myelofibrosis (MF) and may contribute to ineffective hematopoiesis, progressive marrow fibrosis, and disease-associated cytopenias. The osteoprotegerin/receptor activator of nuclear factor kappa-B ligand (OPG/RANKL) pathway, a major regulator of bone turnover with additional roles in immune and hematopoietic regulation, may therefore be relevant to the pathobiology of myeloid neoplasms. Although abnormalities in bone metabolism have been described in MF, the systemic profile of OPG and RANKL and their potential clinical significance in Philadelphia chromosome-negative myeloid neoplasms have not been well characterized. Thus, the aim of this study was to investigate circulating soluble OPG and RANKL levels in patients with Philadelphia chromosome-negative myeloid neoplasms and to explore their association with disease subtype, hematological characteristics, and overall survival.

METHODS: 32 patients (median age 65 years, range 39-85, 17 men, 15 women) diagnosed with Ph chromosome-negative (-) MPNs [polycythemia vera (PV) n=4, essential thrombocythemia (ET) n=15, MF n=8, and MDS/MPN overlap n=5] were included after informed consent. Frozen serum samples were analyzed for soluble OPG and RANKL using ELISA (DuoSet R&D Quantikine) according to the manufacturer's instructions. Fifteen healthy individuals served as controls. Median values of patients were used as cut-offs; values above the median were defined as high. The OPG/RANKL ratio was calculated to assess pathway balance. Median overall survival (OS) of the cohort was 45 months (range 3-208). Statistical analysis was performed using SPSS v29.

RESULTS: Patients with MF exhibited significantly higher OPG levels (median, 1922.54 pg/mL; range, 27-8517.18) compared with other MPN subtypes (median, 889 pg/mL; range, 0-2114; p=0.023) and healthy individuals (median, 830 pg/mL; range, 61-2025; p=0.005). Median RANKL levels in MF were 284.47 pg/mL (range, 0-1401.13), compared with undetectable levels in other MPNs (range, undetectable-2261.67; p=0.001) and 12 pg/mL in controls (range, 0-783; p=0.001). The median OPG/RANKL ratio was 654 (range, 2-20015) in MF, 13.5 (range, 1-2114) in other MPNs, and 54.61 (range, 0-2024) in healthy individuals. One patient with MF who progressed to acute myeloid leukemia (AML) 14 months after diagnosis had a particularly high OPG level of 2519.91 pg/mL. Neither OPG nor RANKL levels, nor the OPG/RANKL ratio, were significantly associated with overall survival (p=0.404, p=0.378, and p=0.291, respectively). Higher OPG levels were significantly correlated with lower hemoglobin levels (r=–0.414, p=0.020).

CONCLUSION: Our findings demonstrate significant alterations of the circulating OPG/RANKL axis in Philadelphia chromosome-negative myeloid neoplasms, particularly in myelofibrosis. Higher OPG levels were associated with lower hemoglobin levels, while OPG, RANKL, and the OPG/RANKL ratio were not significantly associated with overall survival. The relatively unequal numbers of patients across MPN subgroups may have limited the statistical power of the OS analysis. Further studies are warranted to validate these findings.

P11. VALIDATION OF THE IMS/IMWG CONSENSUS GENOMIC STAGING OF HIGH-RISK MULTIPLE MYELOMA IN PATIENTS WITH RENAL IMPAIRMENT

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OBJECTIVE: The novel IMS/IMWG high-risk multiple myeloma (HRMM) criteria utilize serum beta 2-microglobulin (Sb2m) as a marker of tumor burden, but exclude its use in patients with renal impairment (RI; creatinine ≥1.2 mg/dL) due to potential confounding.
METHODS: We analyzed consecutive patients with newly diagnosed multiple myeloma (NDMM) who were treated at a tertiary academic center. RI was defined as creatinine ≥1.2 mg/dL.
RESULTS: Among 1,209 patients, 305 (25.2%) were classified as high-risk per the novel IMS/IMWG criteria, demonstrating an 81% higher risk of death (HR=1.81, p <0.001). At baseline, 419 (34.7%) patients had RI. After adjusting for baseline RI in the multivariate analysis, the novel HRMM criteria retained their prognostic significance. Within this RI cohort, 272 (64.9%) individuals presented with isolated high Sb2m (≥5.5 mg/L) without high-risk cytogenetics and were classified as standard risk. Those patients demonstrated a dismal prognosis compared to standard-risk patients without elevated Sb2m regardless of renal function (aHR=2.61, p=0.009). In exploratory analyses focusing on those with underlying MM-cast nephropathy (Bence-Jones proteinuria, n=226; iFLCr >500, n=135), the majority of patients with RI (n=166, 73.5% and n=96, 71.1%, respectively) exhibited elevated Sb2m but were classified as standard risk. Those subgroups showed also inferior survival compared to those with normal Sb2m and no high-risk features (aHR=3.95, p=0.017 and aHR=6.76, p=0.011, respectively).
CONCLUSION: The novel IMS/IMWG criteria retain their prognostic value in patients with RI. Those with high myeloma burden seem to have particularly adverse prognosis even in the absence of high-risk cytogenetics.

P12. BURDEN AND CHARACTERISTICS OF INFECTIONS IN PATIENTS TREATED WITH BISPECIFIC ANTIBODIES AND THE IMPACT OF IMMUNOGLOBULIN REPLACEMENT

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OBJECTIVE: Bispecific antibodies (BsAbs) targeting BCMA or GPRC5D have significantly improved outcomes inrelapsed/refractory multiple myeloma (RRMM) but are associated with increased infection risk.In this analysis we aimed to describe infection incidence and characteristics as well as the role of Ig replacement in a cohort of BsAb treated patients from a single center in Athens, Greece (Department of Clinical Therapeutics).
METHODS: The analysis included 108 consecutive patients with RRMM treated with bi-specific antibodies (n=90 targeting BCMA and n=18 GPRC5d) starting treatment between 1/2023 and 4/2025. The data on infections were prospectively collected. All patients received prophylaxis for VZV and PJP; CMV monitoring was individualized based on baseline assessment of viral load.
RESULTS: The median number of prior lines of therapy was 3 (IQR 2-4). The median time on BsAb was 7.5 months (IQR 3.3-16.5) and the median follow up time was 8 months. At least one infection occurred in 71 (65.7%) patients; the cumulative risk of infection (accounting for death or disease progression as competing events) was 52%, 63% and 71% at 3, 6 and 9 months, respectively. This suggests a higher early risk for infection. The median time to first infection was 81 days (95%CI: 45-117) and 75% of infectious episodes occurred within the first 3 cycles of therapy. The most frequent infection sites were upper (26%) and lower (27%) respiratory tract, GI (7%) and urinary tract (5%); the etiology was identified as microbial in 48% and viral in 18%. Most infections were grade 2 (52% of all patients) but in 13% were grade ≥3 (including grade 5 in 5% of the cohort). In 13 (18%) patients BsAb therapy was discontinued (in 5 due to death) after their first infectious episode. Only one patient was neutropenic at the time of 1st infection but 41/71 (58%) had ALC <1000/mm3 and 38% had increased LDH levels. At first infection, 70% of patients achieved disease remission (25% were in CR/sCR, 24% in VGPR, 21% in PR). BCMA targeting BsAbs were associated with higher probability of infections (70% vs 44%, p=0.037); which occurred earlier than in non-BCMA BsAb (median time to 1st infection 74 vs 169 days). 80% of the patients in our cohort received Ig supplementation; 40% started Ig replacement prophylactically (before any infection); 39% of patients with infections were on Ig replacement at the time of 1st infection but 58% had polyclonal IgG < 400 mg/dl at the time of the infection. An infection occurred in 73% of patients not receiving prophylactic Ig supplementation vs 22.5% of patients receiving Ig supplementation (HR:0.14, p<0.001).
CONCLUSION: The risk of infection is significant among patients with MM treated with BsAbs, especially BCMA targeting. Early prophylactic use of Ig supplementation decreases infection burden in patients treated with BsAbs; however, further optimization of prophylactic strategies is required. Physicians and patients should be alert as serious infections can occur despite prophylactic measures.

P13. CIRCULATING TUMOR CELLS AS A PROGNOSTIC BIOMARKER IN NEWLY DIAGNOSED MULTIPLE MYELOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVE: Risk stratification in newly diagnosed multiple myeloma (NDMM) relies on standard clinicopathological staging and cytogenetics. However, traditional staging often requires invasive bone marrow biopsies that may fail to capture spatial disease heterogeneity. Circulating tumor cells (CTCs) serve as a non-invasive "liquid biopsy" reflecting systemic tumor burden, yet their prognostic weight and optimal stratification methods remain unstandardized.

METHODS: A systematic literature search was conducted in PubMed, Scopus, and Cochrane databases through September 29, 2025, following PRISMA guidelines to identify clinical studies evaluating CTCs in NDMM. Pooled estimates and 95% confidence intervals (CIs) were calculated using random effects models. This systematic review and meta-analysis was registered in PROSPERO (ID: CRD420251159350).

RESULTS: Eighteen peer-reviewed studies comprising 5,183 NDMM patients were analyzed. Patients with high or detectable CTCs had a two-fold increased risk of disease progression or death (PFS: pooled HR = 2.13; 95% CI: 1.84–2.46; p < 0.001) and a 2.5-fold higher risk of death (OS: pooled HR = 2.50; 95% CI: 1.98–3.16; p < 0.001) compared to those with low or undetectable levels. Sensitivity analyses restricted to multivariate-adjusted data validated the independent prognostic role of CTCs for both PFS (HR = 2.15, 95% CI: 1.87–2.48; I^2 = 26.6%) and OS (HR = 2.62, 95% CI: 2.02–3.40; I^2 = 20.6%). Between-study heterogeneity was negligible (I^2 = 0.0%) among studies using quantitative, percentage-based cut-offs for both PFS and OS, whereas qualitative "presence vs. absence" stratification yielded high heterogeneity (I^2 = 80.4% for PFS; I^2 = 49.3% for OS). The pooled effect size for OS was significantly larger in the quantitative subgroup compared to the qualitative subgroup (HR = 3.04 vs. 1.95, p = 0.021). Meta-regression revealed that the percentage of patients harboring HRCAs was positively associated with both PFS HRs (estimate = 0.0163, p = 0.015) and OS HRs (estimate = 0.0209, p = 0.037), accounting for 100% of the observed heterogeneity in both endpoints. Exploratory analysis linked high CTCs with key high-risk clinical features, showing significant correlations with ISS-3 (OR = 1.80, 95% CI: 1.06–3.05, p = 0.032), R-ISS-3 (OR = 2.41, 95% CI: 1.54–3.76, p = 0.002), and HRCAs (OR = 1.88, 95% CI: 1.03–3.43, p = 0.042). Trim-and-fill analysis for publication bias confirmed stable and statistically significant pooled effect sizes (PFS adjusted HR = 1.89, 95% CI: 1.59–2.24, p < 0.001; OS adjusted HR = 2.07, 95% CI: 1.61–2.66, p < 0.001). Under GRADE guidelines, PFS and OS outcomes were classified as high-certainty evidence, while R-ISS-3 correlation was moderate-certainty, and ISS-3 and HRCA associations were low-certainty due to heterogeneity.

CONCLUSION: This large-scale meta-analysis provides high-certainty evidence validating quantitative CTC assessment as a robust, independent prognostic biomarker in NDMM. Clinical utility is maximized when CTCs are quantified as a continuous/percentage-based metric rather than a binary variable. Reflecting tumor spatial dynamics and genetic aggression, standardized quantitative CTC thresholds should be integrated into routine clinical practice to refine risk stratification and guide risk-adapted treatment strategies.

P14. CIRCULATING TUMOR CELLS AS A PROGNOSTIC BIOMARKER FOR PROGRESSION FROM PRECURSOR STATES TO SYMPTOMATIC MULTIPLE MYELOMA: A SYSTEMATIC REVIEW AND POOLED ANALYSIS

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OBJECTIVE: Accurately predicting the risk of progression to symptomatic multiple myeloma from precursor states is critical to optimize patient management and early intervention strategies. In this context, liquid biopsy with circulating tumor cells (CTCs) has emerged as a promising, minimally invasive biomarker that may reflect aggressive biology.

METHODS: A systematic search was conducted in the PubMed, Web of Science, and Scopus databases, to identify studies on the prognostic impact of CTCs in MGUS and SMM, from inception until December 31, 2025. The primary endpoints were progression-free survival (PFS) and time-to-progression (TTP). To overcome the limitations of proportional hazards models in cohorts with zero progression events, we utilized the Restricted Mean Survival Time difference (ΔRMST) as our primary effect size. Pooled estimates were calculated using inverse-variance weighted random-effects models.

RESULTS: A total of 483 articles were identified, which - after the screening process - ultimately resulted in 7 eligible records of 7 studies with non-overlapping populations to be included. Across these studies, the cutoffs utilized to define a high-risk circulating tumor burden were heterogeneous, including strict cellular counts, relative percentages, and absolute concentrations. Thus, all pooled effect outcomes compared CTC positivity vs negativity to ensure at least 3 records per outcome studied. To evaluate the prognostic value of CTCs in MGUS, a pooled analysis evaluated the ΔRMST at 24 months for PFS incorporating data from Vasco-Mogorrón et al (2021) and Uehara et al (2025). The pooled ΔRMST at 24 months was -1.98 months (95% CI: -4.52 to 0.55; p = 0.126), compared to with no observed heterogeneity (I2 = 0.0%). In SMM, the 24-month PFS ΔRMST pooled analysis included cohorts from Dutta et al (2023), Vasco-Mogorrón et al (2021), and Uehara et al (2025). The pooled ΔRMST of -2.87 months (95% CI: -5.99 to 0.24;p = 0.071) indicates that CTC-positive SMM patients lost an average of 2.87 months of PFS within the first two years, albeit results being marginally non-significant. Moderate heterogeneity was observed (I2=63.1%). When isolating TTP endpoints at 24 months, the pooled analysis of studies by Sanoja-Flores et al (2018), Gonsalves et al (2017), and Termini et al (2022) demonstrated a highly significant clinical impact in SMM patients. CTC positivity at baseline resulted in a pooled ΔRMST at 24 months of -6.39 months (95% CI: -9.65 to -3.12; p < 0.001), indicating a substantial and statistically significant increased risk of progression to active MM within the two-year risk window. Moderate heterogeneity was observed (I2 = 51.2%). Moreover, in the Vigliotta et al (2024) study, a higher level of detectable CTCs was significantly correlated with earlier transformation to active MM (p = 0.042), but IPD could not be extracted and thus the study was not pooled with the aforementioned ones.

CONCLUSION: Among patients with SMM, the presence of CTCs seems to predict early disease dissemination and an elevated risk of progression to active MM within 2 years. The significant ΔRMST reduction of over 6 months in TTP highlights CTCs as a key variable for incorporation into modern staging algorithms to identify candidates for early intervention.

P15. HIGH MRD NEGATIVITY AND PROJECTED LONG-TERM PROGRESSION-FREE SURVIVAL WITH BELANTAMAB MAFODOTIN AND LENALIDOMIDE/DEXAMETHASONE IN TRANSPLANT-INELIGIBLE, INTERMEDIATE FIT AND FRAIL, NEWLY DIAGNOSED MULTIPLE MYELOMA

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OBJECTIVE: The aim of this study was to evaluate safety, tolerability, and clinical activity of belantamab mafodotin (belamaf) plus lenalidomide and dexamethasone (Rd) (BelaRd) in transplant ineligible newly diagnosed multiple myeloma (TI-NDMM) patients (pts).

METHODS: BelaRd trial (NCT04808037) was a phase 1/2, open label study. PFS was extrapolated using parametric survival models. Projected median PFS (mPFS) and 95% confidence intervals (CIs) were estimated for the overall population and the RP2D subgroup.

RESULTS: At clinical cut off 15th May 2026, in Part 1, 21 pts (58.3%) remained on treatment, while 15 (41.7%) were discontinued. Reasons for discontinuation included AEs/SAEs (16.7%), and withdrawal of consent, death, and Disease progression (8.3% each). In Part 2, 19 patients (63.3%) remained on treatment and 11 (36.7%) discontinued. At baseline, ECOG PS was 1/2 in 52.8%/5.6% in part 1 and 56.7%/3.3% in part 2. R-ISS II/III in 75%/8.3% and 63.3%/10% of pts in part 1 and 2, respectively. High-risk cytogenetics was present in 8.3% of pts in part 1 and 16.7% pts in part 2. Median follow up was 53.7 months (range 3.2- 62.0) in part 1 and 37.1 months (range 3.9-44.0) in part 2. Median treatment duration was 52.9 months (range 2.8-61.7) and 36.2 months (range 3.8-43.9) for part 1 and 2 respectively. Median belamaf exposure was 14.5 doses in part 1 and 12 doses in part 2. Median dose intensity was 0.5 mg/kg Q4W in both the parts with median relative dose intensity of 60.7% (range 17.6-95.7) and 40.4% (range 27.9-73.5), respectively. Overall response rate (ORR) (≥PR) was 100% in part 1 (sCR, 47.2%; CR, 13.9%; VGPR, 27.8%; and PR, 11.1%) and 93.3% in group A and 100% in group B of part 2. The median time to first response was 1.0 month (range 0.9-2.9) and time to best response was 19.2 and 12.6 months (range 1.0-47.2) and (range 1.1-30.7) for part 1 and 2, respectively. Overall MRD negativity at the time of CR in part 1 and 2 was achieved in 86.4% (19/22) and 94.1% (16/17) of MRD evaluable pts, respectively. The 12- and 24-months sustained MRD negativity rates were 66.6% (8/12) and 80% (12/15) of MRD evaluable pts, respectively. Overall median PFS & TTP were not reached. PFS rate at 24 months was 79.8% (95% CI 67.7-87.7) and for RP2D was 78.0% (95% CI 61.9-87.9). The TTP at 24 months was 98.2% (95% CI 88-99.8) and 97.2% (95% CI 81.9-99.6) for overall and RP2D population, respectively. Projected mPFS for the overall pts ranged from 84.6-105.3 months (7-8.7 years) and for RP2D ranged from 83.9 to 99.5 months (6.9-8.3 years). OS rate at 24 months was 81.6% (95% CI 69.8-89.1) and for RP2D was 80.7% (95% CI 65.1-89.9). Dose holds occurred in 34.3% in part 1 (OAEs) and in 22.7% in Gr A (OAEs) versus 2.7% in Gr B (VRA-guided).

CONCLUSION: Belamaf plus Rd demonstrated rapid, deep, and durable responses in transplant-ineligible intermediate-fit/frail NDMM, with high ORR, sustained disease control, and high PFS and MRD negativity rates.

P16. SUCCESSFUL TREATMENT WITH RITUXIMAB AFTER LOSS OF RESPONSE TO ELTROMBOPAG IN AN ELDERLY PATIENT WITH SEQUENTIAL AIHA AND REFRACTORY ITP: A CASE REPORT

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OBJECTIVE: CASE PRESENTATION An 84-year-old female with a known history of autoimmune hemolytic anemia presented with petechial bleeding on her arms. Physical examination was unremarkable except for petechiae. There was no splenomegaly. Laboratory tests revealed isolated thrombocytopenia with normal hemoglobin and white blood cell count and there was no sign of hemolysis. Other autoimmune diseases were excluded. She was diagnosed with ITP and she was successfully treated with initial corticosteroid therapy. At 6 months, she relapsed. Due to advanced age and high surgical risk, splenectomy could not be performed. Eltrombopag was started with a good initial response. Fourteen months later, she lost response to eltrombopag. She became refractory to both IVIG and corticosteroids. A bone marrow aspiration and biopsy were performed and they revealed increased megakaryocytes with no other pathological findings. Rituximab therapy (375 mg/m2 once a week for 4 consecutive weeks) was initiated. At week 6, platelet count increased to over 50,000/μL.

METHODS: TBA

RESULTS: DISCUSSION This case illustrates several key points. First, sequential autoimmune cytopenias can occur without meeting criteria for Evan's syndrome. Second, the management of ITP in very elderly patients is challenging due to comorbidities and treatment-related risks. The finding of increased megakaryocytes on bone marrow examination confirmed peripheral immune destruction as the mechanism of thrombocytopenia and excluded other causes such as myelodysplasia. Loss of response to thrombopoietin receptor agonists is an emerging clinical problem. When combined with refractoriness to IVIG and steroids, treatment options become limited. Our case suggests that rituximab can be an effective rescue therapy in this setting, even in patients over 80 years old. This supports the use of B-cell depletion therapy after TPO-RA failure in selected elderly patients.

CONCLUSION: Rituximab may be considered as a viable option for elderly patients with refractory ITP following eltrombopag failure. Bone marrow examination is important to confirm the diagnosis and exclude other causes. REFERENCES 1. Provan D, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood. 2010;115(2):168-186. 2. Moulis G, et al. Epidemiology of incident immune thrombocytopenia: a nationwide population-based study in France. Blood. 2014;124(22):3308-3315. 3. Khellaf M, et al. Safety and efficacy of rituximab in adult patients with chronic immune thrombocytopenia: results of a prospective registry 2 years after a first course of rituximab. Blood. 2014;123(17):2678-2687. 4. Al-Samkari H, et al. Thrombopoietin receptor agonists in the treatment of refractory immune thrombocytopenia: A real-world experience. Am J Hematol. 2018;93(1):83-90. 5. Audia S, et al. Evans syndrome in adults: A retrospective study of 114 patients. Medicine (Baltimore). 2017;96(21):e6872.

P17. OPERATIONALIZING BISPECIFIC ANTIBODY THERAPY IN VULNERABLE PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA: A REAL-WORLD INDIVIDUALIZED STEP-UP APPROACH

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OBJECTIVE: Patients with frailty or reduced physiological reserve are underrepresented in pivotal trials of bispecific antibodies for relapsed/refractory multiple myeloma (RRMM). We evaluated the feasibility, safety, and early clinical activity of a pre-planned, individualized step-up strategy specifically among patients classified as intermediate-fit or frail.

METHODS: This focused retrospective analysis included patients with RRMM classified as intermediate-fit or frail who initiated talquetamab or elranatamab at a single hematology center. Fit patients from the broader institutional cohort were excluded. Before treatment initiation, step-up administration and subsequent dosing intensity were individualized according to performance status, frailty, comorbidities, organ function, and anticipated treatment-related risk. Treatment-delivery parameters, response, cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), grade ≥3 infections, and treatment continuation were evaluated.

RESULTS: Nine patients were included, of whom four (44.4%) were intermediate-fit and five (55.6%) were frail. Median age was 63 years (range, 56-74). Six patients (66.7%) had an Eastern Cooperative Oncology Group performance status ≥2, including three (33.3%) with performance status 3-4. Patients had received a median of four prior treatment lines (range, 1-8); all were triple-refractory, four (44.4%) were penta-refractory, and all were CAR T-cell-naïve. An individualized modification of the conventional step-up strategy was implemented in all patients. Documented components included planned extension of intervals between step-up doses in three patients (33.3%) and reduced dose or dosing intensity in three (33.3%); two patients (22.2%) underwent both modifications. All patients received structured inpatient monitoring during step-up administration. The overall response rate was 77.8% (7/9), with responses ≥very good partial response achieved in 44.4% (4/9). Any-grade CRS occurred in five patients (55.6%); only one experienced grade 2 CRS, and no grade ≥3 CRS was observed. One patient developed grade 1 ICANS, and one experienced a grade ≥3 infection. At data collection, six patients (66.7%) remained on treatment.

CONCLUSION: A pre-planned, individualized step-up approach enabled bispecific antibody administration with encouraging early activity and manageable toxicity in intermediate-fit and frail patients with heavily pretreated RRMM. Flexible scheduling, individualized dosing intensity, and structured monitoring may facilitate access to bispecific antibodies for patients insufficiently represented in pivotal trials. Larger prospective studies are required to validate these findings.

P18. MIDOSTAURIN IN FLT3+ ACUTE MYELOID LEUKEMIA (AML-FLT3+): DATA OF EVERYDAY CLINICAL PRACTICE

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OBJECTIVE: Midostaurin (MID) is a multi-targeted kinase inhibitor, effective in FLT3 gene mutations, both ITD (internal tandem duplication) and TKD (tyrosine kinase domain). The introduction of MID in 1st line intensive chemotherapy (IC) became a standard of care, based on the RATIFY trial: statistically significant improvement was found in overall survival (OS), median: 75 months for MID plus IC vs 26 months for IC, 5-year OS: 51,4% vs 44,3%, p=0.009 accordingly. No difference was observed in severe adverse events apart from QTc prolongation. Nonetheless, cardiotoxicity and increased incidence of fungal infections were reported in Real world data (RWD). As it is widely recognized, RWD differ from clinical trial results due to patients' selection.
METHODS: We conducted a retrospective analysis of AML-FLT3+ patients treated with MID in everyday clinical practice.
RESULTS: From 406 AML patients, 99 were positive for FLT3 mutations (FLT3-ITD+ 90, FLT3-TKD+ 9). Nine patients were excluded due to cytogenetic alterations (t8;21 2, complex 5, no metaphasis 2). In total, 90 FTL3+ patients were studied (41 men, 49 women) with median age 53(16-75) years and median WBC 38.000 (2.000-25.000)/μl. 42/90 had monocytic AML, 10/90 had secondary AML (sAML), 74/90 patients had no cytogenetic alterations and 16/90 had intermediate risk karyotype with the majority (8/16) expressing +8. NPM1 mutations coexisted in 42/60 patients who were tested, 18/30 (60%) treated with MID and 22/32 (69%) without MID. In total 31/90 patients received MID, median age 53years, FLT3-TKD+ 8/31 (25,8%). In comparison to those treated without MID, no significant difference was observed in complete response (CR) rate (27/31, 87% with MID vs 48/59 81% without MID, p=ns). However, outcome differed significantly: 5-year disease free survival (DFS) was 48% vs 23%, p=0.037 and 5-year OS 70% vs 28,4%, p=0.008, accordingly. From the MID group, more patients underwent allogeneic hematopoietic stem cell transplantation (AlloHCT), 11/31 (35.2%) vs 17/59 (29%), p=0.42. The survival analysis was recalculated with censoring in AlloHCT and still remained superior in the MID group: 5-year DFS 53.5% vs 15%, p=0.01, 5-year OS 64% vs 15%, p=0.006, accordingly. Then AML FLT3-ITD+ patients were compared with intermediate risk AML patients who were FLT3-, NPM1- and no difference in outcome was observed: 5-year DFS was 48% vs 49,6%, p=0.64, 5-year OS 64% vs 54.5%, p=0.52, accordingly. Multivariate analysis (Cox regression) for DFS showed only sAML as an important factor, whereas for OS apart from sAML, MID regimen and AlloHCT were also important factors. The addition of MID in IC was generally well tolerated, with gastrointestinal adverse events, QTc prolongation observed in 3 timelines, and importantly in 3 patients ejection fraction was affected. No increase in fungal infections was observed.
CONCLUSION: In conclusion, the addition of midostaurin in IC was safe and improved the outcome of FLT3+ AML, so that, in combination with allogeneic transplantation it is indeed a standard risk AML.

P19. T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA IN ADULTS: SINGLE CENTER LONG-TERM OUTCOMES

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OBJECTIVE: T-cell acute lymphoblastic leukemia (T-ALL) is less common than B-ALL, accounting for approximately 15% of ALL cases in children and 25% in adults. Consequently, clinical data on patients with T-ALL remain relatively limited.

METHODS: We retrospectively analyzed the clinical characteristics and outcomes of patients with T-ALL treated at our center over the past two decades and compared them with those of patients with B-ALL.

RESULTS: A total of 75 patients with T-ALL (28.5% of ALL cases) were included, 21 females/ 54 males, median age 32 (14-71) years. At diagnosis, the median white blood cell (WBC) count was 11600/μL (range 2200-355000), median LDH 650U/L, median hemoglobin 10g/dL, and median platelet (PLT) count 70000/μL. Baseline characteristics were comparable to B-ALL patients, except for the significantly higher proportion of males in the T-ALL group ($p = 0.015$). The prognostic significance of cytogenetic abnormalities in T-ALL has not yet been fully established. Among 70 patients with available cytogenetic data, 28 had a normal karyotype and 42 abnormal. Recurrent abnormalities were observed in 23 patients. Favorable-risk abnormalities, including t(7;10)(q34;q24) and t(10;14)(q24;q11), were identified in 8 patients, whereas adverse cytogenetic abnormalities, including complex karyotype, t(v;11q23), and t(v;8q24) were detected in 13 patients. Complete remission (CR) following induction was achieved in 65/75 patients (86.7%). Eight patients (10.6%) had refractory disease, while two patients died before completing induction therapy. Among patients achieving CR, 20/65 (30.7%) subsequently relapsed. The 5-year disease-free survival (DFS) was 55.6% for patients younger than 35 years, 46.6% for those aged 35-60 years, and 53% for patients >60 years (n=5). The corresponding 5-year overall survival (OS) rates were 65.1%, 47.5%, and 53%, respectively ($p = 0.61$). As expected, patients who achieved early complete remission (CRearly) had significantly better outcomes, with 5-year DFS 72% versus 26% ($p < 0.001$) and 5-year OS 77.8% versus 38.5% ($p = 0.001$). Furthermore, the impact of L-asparaginase dose on OS was found to be highly significant: 5-year OS for patients who received no L-asparaginase, intermediate dose, or high cumulative dose (>80,000 IU/m^2) were 17%, 65.3%, and 72.3%, respectively ($p < 0.001$). Twenty-six patients underwent allogeneic hematopoietic stem cell transplantation (allo-HSCT), including 13 in first complete remission. Transplantation did not have a statistically significant impact on survival, possibly because most younger patients were treated with pediatric protocol and less frequently underwent transplantation. In multivariable analysis, the cumulative L-asparaginase dose was the only significant prognostic factor for both DFS and OS. Compared with 188 patients with B-ALL, outcomes appeared numerically superior for T-ALL, although with no statistically significant difference (5-year OS: 57.3% vs. 50.5%; 5-year DFS: 50.5% vs. 41.6%; $p = 0.27$).

CONCLUSION: In conclusion, adult T-ALL does not differ substantially from B-ALL with respect to baseline characteristics or clinical outcomes. However, given the recent therapeutic advances in B-ALL—including frontline blinatumomab, third-generation tyrosine kinase inhibitors (TKIs), and chimeric antigen receptor T-cell (CAR-T) therapy—the prognosis of B-ALL is expected to improve considerably. Therefore, the development of novel therapeutic approaches for T-ALL remains an urgent unmet clinical need.

P20. RECOGNIZING MYELOID NEOPLASIA BEHIND INFLAMMATORY SKIN LESIONS: A CASE OF HIGH RISK MDS WITH COEXISTENT MBL

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OBJECTIVE: Autoimmune disorders (ADs) are increasingly recognized as part of the clinical and biological spectrum of myelodysplastic syndromes (MDS). Patients with concomitant MDS and AD tend to present at a younger median age and exhibit a less pronounced male predominance than those with isolated MDS. Certain MDS subtypes appear more frequently associated with ADs, particularly MDS with single lineage dysplasia (MDS-SLD) and MDS with excess blasts (MDS-EB). Bone marrow biopsies often reveal clonal $CD8^+$ T cell expansion, which is linked to more profound cytopenias, especially in patients with trisomy 8. This report details a case of MDS, identified after the patient developed a new onset rash that led to further diagnostic evaluation.

METHODS: A 90 year old man presented to the emergency department following the incidental finding of anemia during outpatient testing, which had been performed after the sudden onset of a cutaneous rash involving the trunk and extremities, without accompanying systemic symptoms. Laboratory evaluation revealed neutropenia, normochromic normocytic anemia, and mild thrombocytopenia. Peripheral blood smear examination demonstrated dysplastic features in neutrophils and platelets, as well as a small population of monomorphic lymphoid cells. Peripheral blood immunophenotyping identified a small clonal B cell population with partial expression of CD20 and CD79b and weak κ light chain restriction. These findings at first raised suspicion for a cutaneous B cell non Hodgkin lymphoma.

RESULTS: A skin biopsy was performed twice, both times revealing changes consistent with psoriasiform chronic spongiotic dermatitis, without any evidence of B NHL infiltration. Computed tomography scans showed no lymphadenopathy or hepatosplenomegaly. Bone marrow biopsy demonstrated 10-12% infiltration by $CD34^+$ myeloblasts, with no monoclonal lymphoid population identified. Cytogenetic analysis revealed 47, XY, +8, while next generation sequencing results are pending. Based on these findings, the diagnosis of MDS/AML according to ICC 2022, classified as very high risk by IPSS R, was established, with a concurrent incidental CD5 negative non-CLL MBL identified in the peripheral blood. The patient initiated treatment with azacitidine and is currently receiving the third cycle, showing improvement in hematologic parameters and partial regression of the rash. For the residual cutaneous manifestations, initiation of anti IL 23 monoclonal antibody therapy is planned.

CONCLUSION: Clinicians should maintain a high index of suspicion for underlying myeloid neoplasia when elderly patients present with unexplained cytopenias accompanied by possibly immune-mediated symptoms. This case demonstrates how seemingly benign dermatologic findings can mask high risk MDS, emphasizing the importance of thorough hematologic evaluation, whenever cytopenias persist or lack a clear etiology. Early recognition allowed timely initiation of azacitidine therapy, leading to improvement in both hematologic parameters and cutaneous manifestations, underscoring the value of prompt, disease directed treatment in such presentations.

P21. TECLISTAMAB AND ELRANATAMAB IN THE REAL WORLD PROVED EQUALLY EFFECTIVE AND SAFE. EFFECTIVENESS AFTER PRIOR EXPOSURE TO ANOTHER ANTI-BCMA AGENT IS NOT COMPROMISED; INDIRECT COMPARISON OF STUDIES USING SINGLE-ARM METANALYSIS AND THE GENERALIZED LINEAR MIXED MODEL

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OBJECTIVE: Teclistamab and elranatamab are profoundly effective in heavily pre-treated relapsed myeloma patients according to phase II clinical trials but infections are still a major concern. In the real- world more fragile populations are treated with anti-BCMA bispecifics and their efficacy and safety is questionable.
METHODS: Here-in we are performing a single arm meta-analysis of efficacy and safety of both teclistamab (n=2357 patients) and elranatamab (n=419 patients) in a summit of real-world cohorts and we are further comparing indirectly teclistamab and elranatamab by using the general linear mixed model method.
RESULTS: Overall response rates (ORR) in teclistamab treated patients was 63% and ≥ VGPR achieved in 48%. In the elranatamab arm ORR was 57% and ≥VGPR rate was 43%. Efficacy after another prior anti-BCMA agent was reported only in the teclistamab arm and was ORR 52% and ≥ VGPR 42%. Cytokine release syndrome (CRS) with teclistamab and elranatamab was at the rate of 50% and 43% while severe ≥ grade 3 infections in the rate of 26% and 23% respectively. Then we segregated patients according to type of anti-BCMA treatment received in prior lines of therapy ADC (n= 224 pts) vs CART (n= 443 pts). The OR (95% CI) for ORR was with ADC= 0,58 (0,49-0,67) and for CART= 0,52 (0,42-0,63) and after comparing them with the GLMM method; OR (95% CI) =1.292, (0.789-2.115), p-value=0.281. Although not statistically significant the ≥ VGPR rate is better when prior anti-BCMA agent was ADC. The OR (95% CI) for ≥ VGPR was ADC= 0,45 (0,34-0,56) and for CART= 0,36 (0,28-0,45) and after comparing them with the GLMM method; OR=1.561 (0.936-2.603), p-value=0.082.
CONCLUSION: Teclistamab and elranatamab show remarkable efficacy and accepted safety in the real-world, reproducing results from the clinical trials. Indirect comparison of teclistamab and elranatamab in real-world cohorts, found them equally effective and safe. Notably, their effectiveness after prior exposure to another anti-BCMA agent is not severely compromised.

P22. CAN ATTRIBUTING SYMPTOMS TO BODYBUILDING DELAY A LYMPHOMA DIAGNOSIS? SPLENIC DIFFUSE RED PULP SMALL B-CELL LYMPHOMA IN A 22-YEAR-OLD MAN

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OBJECTIVE: Splenic diffuse red pulp small B-cell lymphoma (SDRPL) is a rare, indolent mature B-cell neoplasm accounting for less than 1% of non-Hodgkin lymphomas and about 10% of B-cell lymphomas found in splenectomy specimens. It mainly involves splenic red pulp but can also affect bone marrow, peripheral blood, and hilar lymph nodes. WHO-HAEM5 recognizes SDRPL as a distinct entity overlapping clinically, morphologically, and immunophenotypically with hairy cell leukemia (HCL), splenic B-cell lymphoma/leukemia with prominent nucleoli (SBLPN), and splenic marginal zone lymphoma (SMZL); diagnosis requires integrating blood morphology, flow cytometry, marrow findings, and splenic histopathology. SDRPL mainly affects older adults; we report this case as our 22-year-old patient had attributed his weight loss, night sweats, and fatigue to bodybuilding.

METHODS: A 22-year-old man with no comorbidities presented with diarrhea and fever, having attributed weight loss (>20% of body weight), night sweats, fatigue, and abdominal fullness from splenomegaly to a year of bodybuilding. Examination showed conjunctival pallor and massive splenomegaly. Complete blood count showed white blood cells 255.7×10^9/L, hemoglobin 8.4 g/dL, hematocrit 28.8%, platelets 124×10^9/L; 76% of leukocytes (194.3×10^9/L) were large unstained cells, absolute lymphocytes 53.3×10^9/L, LDH 549 U/L. The smear showed atypical villous lymphocytes. Flow cytometry did not support classic HCL. Bone marrow biopsy showed extensive intrasinusoidal infiltration by small atypical B cells, compatible with HCL-v/SBLPN; cell size argued against B-PLL, and variable CD27/absent CD200 against MZL. BRAF V600E was negative; cytogenetics showed IGH-locus amplification. Disease stabilized after rituximab-cladribine. Splenectomy confirmed SDRPL histopathologically (Figure 1). At 18 months, he remained asymptomatic and continued training.

RESULTS: SDRPL typically presents in older adults, with median ages of 66-79 years and much lower leukocyte counts in pooled series; despite our patient's extremes, his splenomegaly, villous lymphocytes, cytopenias, and marrow infiltration matched the typical SDRPL pattern. Distinguishing SDRPL from HCL, SMZL, and SBLPN remains difficult, and diagnosis ultimately relied on splenic histopathology. Similar overlap has been reported in older patients with protracted courses, unlike our patient's acute presentation. SDRPL's molecular landscape is heterogeneous, and the IGH amplification found here lacks specific weight without further characterization. No standardized treatment exists; options include observation, splenectomy, and rituximab-based regimens, with outcomes linked to age, marrow involvement, and blood counts. His young age may be favorable, but extreme leukocytosis and marrow involvement counter this, and early transformation to large B-cell lymphoma has been reported, so 18 symptom-free months is reassuring but not conclusive. What makes this case unusual is the combination of extreme leukocytosis, massive splenomegaly, and B symptoms attributed to exercise, which did not cause the disease but shows how easily such symptoms can be folded into a training narrative, delaying recognition of serious hematologic disease in young, active patients.

CONCLUSION: SDRPL can present at a young age with extreme leukocytosis. Diagnosis required peripheral blood, bone marrow, and splenic histopathology together. New weight loss, night sweats, or fatigue in young, active patients warrant the same clinical scrutiny as in anyone else, regardless of how plausible a lifestyle explanation seems.

P23. THE ROLE OF BETA-2 MICROGLOBULIN IN PREDICTING TIME TO FIRST TREATMENT IN CHRONIC LYMPHOCYTIC LEUKEMIA: A RETROSPECTIVE PILOT STUDY

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OBJECTIVE: Chronic lymphocytic leukemia (CLL) follows a highly variable clinical course, and several scoring systems, including the CLL-IPI, IPS-E, and CLL-WONT, have been developed to predict time to first treatment (TTFT). This retrospective pilot study investigated the relationship between clinical, genetic, and laboratory variables and TTFT in a CLL cohort, focusing on the relative importance of B2M.

METHODS: Twenty-two patients with CLL were included. TTFT was defined as time from diagnosis to first treatment; untreated patients were censored at last follow-up. Fourteen patients received treatment and 8 remained untreated. Age, sex, Rai/Binet stage, IGHV mutation status, TP53 mutation, trisomy 12, del(11q), del(13q), hemoglobin, platelet count, leukocyte subtypes, monocyte-to-lymphocyte ratio, LDH, CD38, ZAP70, and B2M were analyzed by univariate Cox regression. Because only 14 treatment events occurred, multivariable analysis was not performed and results were considered preliminary.

RESULTS: Median age at diagnosis was 62 years (range 36–84); 59.1% were male. Rai stage was 0–III in 36.4%/31.8%/18.2%/13.6%, and Binet stage A–C in 36.4%/59.1%/4.5%. Median baseline hemoglobin was 13.35 g/dL, platelets 178.5×10^9/L, white blood cells 21.63×10^9/L, absolute lymphocytes 15.04×10^9/L, LDH 184 U/L, and B2M 3.47 mg/L. On univariate analysis, age, sex, Rai stage, Binet stage, IGHV status, TP53 mutation, trisomy 12, del(13q), del(11q), CD38, and ZAP70 were not significantly associated with TTFT. Each 1 mg/L increase in B2M was associated with a 52.2% higher rate of treatment initiation and shorter TTFT (hazard ratio [HR] 1.522; 95% CI 1.040–2.227; p=0.031), the only statistically significant association found. Hemoglobin, platelet count, absolute neutrophil count, and neutrophil percentage showed non-significant trends toward shorter TTFT with worsening values (p=0.056–0.069). Baseline B2M was the only variable significantly associated with TTFT, consistent with its established role in CLL-IPI and with the CLL-WONT system, in which B2M above 4 mg/L independently predicted shorter TTFT alongside age, stage, LDH, lymphocyte count, IGHV status, and del(11q)/del(17p). Because B2M is renally cleared, its predictive value for TTFT may be attenuated in patients with impaired renal function, even though its association with overall survival appears more robust. The lack of significance for IGHV, TP53, cytogenetics, and stage should not be read as evidence against their prognostic relevance, since larger cohorts have established these associations; our small sample and limited treatment events likely reduced power. Similarly, the borderline trends in hemoglobin, platelets, and neutrophil parameters may reflect disease burden or marrow involvement but cannot be considered definitive given multiple comparisons and wide confidence intervals. Key limitations include the retrospective design, small sample and event numbers, missing data for some variables, exclusion of renal function from analysis, and inability to perform multivariable analysis; strengths include use of a time-dependent endpoint and joint evaluation of routinely available clinical, genetic, and laboratory variables.

CONCLUSION: Baseline serum B2M level was associated with shorter TTFT in this retrospective pilot cohort, supporting its role as a practical, accessible predictor. Confirmation in larger, prospective, multicenter studies is warranted.

P24. OUR EXPERIENCE WITH ECULIZUMAB IN COLD AGGLUTININ DISEASE REFRACTORY TO MULTIPLE LINES OF THERAPY

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OBJECTIVE: Cold agglutinin disease (CAD) is a rare hematologic disorder and accounts for approximately 15% of the causes of autoimmune hemolytic anemia [1]. In elderly patients presenting with unexplained anemia accompanied by symptoms triggered by cold exposure, CAD should be considered in the differential diagnosis, and in cases of clinical suspicion. While managing this disease is quite challenging, complement inhibitors can be a good option in selected patient groups.

METHODS: A 78-year-old woman presented to us with anemia. Physical examination revealed pallor of the skin and conjunctivae, scleral icterus, and the presence of Raynaud phenomenon. Laboratory evaluation showed a hemoglobin level of 8.8 g/dL, hematocrit 11.4%, mean corpuscular volume 103 fL, white blood cell count 7.96×10^9/L, neutrophils 4.38×10^9/L, lymphocytes 3.0×10^9/L, and monocytes 0.39×10^9/L. Indirect bilirubin was elevated at 2.7 mg/dL, lactate dehydrogenase was 313 U/L, and haptoglobin was decreased. Transferrin saturation was 67%, ferritin 374 ng/mL, vitamin B12 level is 728 pg/mL, and folate level is 20 ng/mL. The DAT was strongly positive for C3d (4+). Complement levels (C3, C4), viral serologies, rheumatologic tests, cultures and cryoglobulins were negative. Peripheral blood smear demonstrated marked erythrocyte agglutination. Given the presence of indirect hyperbilirubinemia, elevated LDH, decreased haptoglobin, positive DAT with C3d positivity, and erythrocyte agglutination on peripheral smear, a preliminary diagnosis of cold agglutinin disease was considered, and a cold agglutinin test was sent, which returned positive. To investigate the underlying etiology, contrast-enhanced computed tomography, as well as FDG-PET imaging, were performed and revealed no evidence of malignancy. Bone marrow aspiration and biopsy showed no findings suggestive of myelodysplastic syndrome; plasma cells accounted for 3% of nucleated cells. The patient was evaluated for multiple myeloma, and an IgM kappa monoclonal gammopathy was detected; she was subsequently diagnosed with MGUS and placed under surveillance. The patient sequentially received rituximab monotherapy, oral cyclophosphamide, rituximab plus bendamustine, and bortezomib; however, no clinical response was achieved with any of these therapies (with folic acid). The patient subsequently underwent three sessions of plasmapheresis, followed by initiation of eculizumab at a dose of 900 mg every two weeks (March 2025). The patient received all recommended vaccinations prior to the initiation of eculizumab therapy. After a total of fourteen months of eculizumab therapy, the patient's anemia and hemolytic parameters have improved, and she is being followed up in an asymptomatic state.

RESULTS: CAD's treatment strategies have increasingly focused on clonal B-cell-directed therapies and complement-targeted approaches. Plasmapheresis aimed at removing circulating pathogenic antibodies also represents a therapeutic option in selected cases [3]. In the present case, B-cell-directed therapies were administered sequentially as first-line strategies; however, no meaningful clinical response was achieved. Despite the use of rituximab plus bendamustine—the regimen associated with the highest reported ORR in B cell targeted therapy our patient failed to achieve an adequate response, prompting a switch to complement inhibition with eculizumab [2].

CONCLUSION: CAD's treatment strategies can be broadly categorized into B-cell-directed and complement-directed therapies. In treatment-refractory cases, switching the therapeutic target may represent a beneficial approach [4].

P25. IMMUNOGENICITY AND SAFETY OF THE RECOMBINANT ADJUVANTED RESPIRATORY SYNCYTIAL VIRUS VACCINE IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA AND MULTIPLE MYELOMA

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OBJECTIVE: Disease- and treatment-related immunosuppression impairs vaccine-induced immune responses in patients with chronic lymphocytic leukemia (CLL) and multiple myeloma (MM). Respiratory syncytial virus (RSV) causes severe, often fatal, lower respiratory infection in patients with hematological malignancies. The efficacy and safety of the recombinant adjuvanted RSV vaccine (Arexvy®) have been demonstrated in immunocompetent older adults, but data in immunocompromised patients, particularly those with CLL and MM, remain limited.

METHODS: We conducted a multicenter study to evaluate the immunogenicity and safety of Arexvy® in adult patients with CLL and MM. Written informed consent was obtained from all participants. Patients were vaccinated with a single intramuscular dose of 0.5 mL of Arexvy® (containing 120 mcg of the recombinant RSV fusion glycoprotein and AS01E, a liposome-based adjuvant system). The primary endpoint of the study was to assess immunogenicity by measuring anti-RSV IgG antibodies (RSV-IgG-Ab) at baseline and 28 days post-vaccination using the commercially available EUROIMMUN panel-IgG assay (Medizinische Labordiagnostika AG, Lübeck, Germany), with sensitivity and specificity of 100% and 96.2%, respectively. Secondary endpoints included assessment of changes in seropositivity, correlation of antibody titers with baseline and treatment characteristics, and vaccine safety. The study was approved by the Institutional Review Boards of the participating centers.

RESULTS: The study included 170 patients (69 with CLL and 101 with MM) with a median age of 74.8 years. Baseline IgG seropositivity was 67.8%, with a median antibody titer of 44.4 RU/mL (0-146.7). Out of the 170 patients, 153 received vaccination (90.0%), and 149 (87.6%) provided a post-vaccination sample. Post-vaccination IgG seropositivity increased to 94.6% ($p<0.001$), with a corresponding increase in RSV-IgG-Ab to 81.8 RU/mL (8.7-158.3, $p<0.001$). Neither pre- nor post-vaccination RSV-IgG-Ab was associated with age, sex, or baseline hematological parameters. Median pre-RSV-IgG-Ab differed significantly according to treatment status, with treatment-naïve and non-actively treated patients exhibiting higher titers than actively treated patients (67.3 vs 31.5 RU/mL, $p<0.001$). Moreover, pre-RSV-IgG-Ab was significantly higher in patients with CLL than those with MM (61.2 vs 29.3 RU/mL, $p=0.001$), but post-RSV-IgG-Ab was higher in MM than in CLL (88.7 vs 73.2 RU/mL, $p=0.027$). A >4-fold increase in antibody titers was observed in 36.7% of patients with MM compared with only 6.7% of those with CLL. In patients with MM (but not CLL), both pre- and post-RSV-IgG-Ab were lower in actively treated patients (21.7 vs 82.1 RU/mL, $p=0.005$, and 87.4 vs 111.7 RU/mL, $p=0.046$, respectively), without any association with prior exposure to rituximab, venetoclax, BTK inhibitors, or daratumumab.

CONCLUSION: Two-thirds of patients had detectable pre-RSV-IgG-Ab (67.8%) that increased to 94.6% after vaccination. Although patients with CLL had higher pre-RSV-IgG-Ab, patients with MM mounted a greater humoral response following vaccination. Moreover, treatment-naïve patients in both groups had higher pre-RSV-IgG-Ab, while actively treated patients had the lowest baseline levels. Active treatment was associated with impaired post-vaccination antibody responses only in MM patients. These findings demonstrate robust humoral immunogenicity of RSV vaccination in patients with CLL and MM, although responses may be attenuated during active therapy.

P26. PRIMARY COLD AGGLUTININ DISEASE PRESENTING AS FEVER OF UNKNOWN ORIGIN WITHOUT EVIDENCE OF HEMOLYSIS: A DIAGNOSTIC CHALLENGE

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OBJECTIVE: Primary cold agglutinin disease (CAD) is a rare complement-mediated autoimmune hemolytic anemia classically characterized by chronic hemolysis and cold-induced circulatory symptoms. However, atypical presentations may delay diagnosis and lead to extensive investigations. We report a patient with primary CAD, presenting as fever of unknown origin in the absence of laboratory evidence of hemolysis.
METHODS: An 87-year-old patient was admitted with persistent fever of unknown origin. A comprehensive diagnostic workup was performed to investigate infectious, autoimmune, malignant, and hematologic causes. The evaluation included immunohematologic testing, microbiological investigations, serum protein electrophoresis, bone marrow examination, and whole-body FDG-PET/CT.
RESULTS: Initial laboratory evaluation demonstrated mild anemia with hemoglobin 10.4 g/dL and a disproportionately low hematocrit of 24.8%, without biochemical evidence of active hemolysis. Lactate dehydrogenase remained between 180 and 250 U/L, total bilirubin was 0.6 mg/dL, haptoglobin was 162 mg/dL, and the reticulocyte count was 0.65%. The direct antiglobulin test was positive for C3c and negative for IgG. Cold agglutinin testing revealed a markedly elevated antibody titer (1:2048). Secondary etiologies of cold agglutinin disease were thoroughly excluded, encompassing infections with Epstein-Barr virus (EBV), cytomegalovirus (CMV), Mycoplasma pneumoniae, as well as lymphoproliferative disorders and other undetected malignancies. Serum protein electrophoresis was normal, bone marrow examination demonstrated reactive changes with erythroid hyperplasia, and FDG-PET/CT showed no evidence of lymphoproliferative disease or occult malignancy. Based on these findings, a diagnosis of primary cold agglutinin disease was established. Treatment with rituximab was initiated, leading to complete resolution of fever. After three doses of rituximab, follow-up laboratory evaluation demonstrated improvement of anemia, with hemoglobin increasing to 10.9 g/dL and hematocrit rising to 30%. No alternative diagnosis emerged during follow-up.
CONCLUSION: Primary cold agglutinin disease may rarely present as fever of unknown origin despite the absence of overt hemolysis. A complement-positive (C3-positive), IgG-negative direct antiglobulin test together with a high cold agglutinin titer should prompt consideration of CAD even when classical markers of hemolysis are absent. Thorough exclusion of secondary causes is essential before establishing the diagnosis of primary CAD. Recognition of this uncommon presentation may facilitate earlier diagnosis and appropriate treatment while avoiding unnecessary investigations.

P27. VARIANTS OF THE PHILADELPHIA CHROMOSOME IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA

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OBJECTIVE: Chronic Myeloid Leukemia (CML) is characterized by the presence of the Philadelphia (Ph) chromosome, arising from a reciprocal translocation between the long arms of chromosomes 9 and 22, resulting in the formation of the BCR::ABL1 chimeric gene. In 2-10% of CML patients, BCR::ABL1 results from a variant of this translocation, in which, in addition to the 9q34 and 22q11 regions, one or more regions of other chromosomes are involved. The aim of this study was to determine the frequency, type, and clinical significance of variants of the t(9;22)(q34;q11), as well as to demonstrate the type and frequency of coexistence of additional chromosomal aberrations (ACAs).

METHODS: Since 1998, 440 diagnostic samples from CML patients were studied by conventional karyotype. Cytogenetic analysis was performed after 24-hour and 48-hour bone marrow culture, and chromosomes were identified by G-banding. Karyotypes were described according to ISCN 2024 nomenclature. Eighteen patients (4%) presented with Ph variant translocations. Eleven were male and 7 female, with a median age at diagnosis of 48 years (range 11-71).

RESULTS: Five patients presented simple variant translocations, involving, in addition to 22q11, one of chromosomes 2, 6, 8, 9, and 14. Thirteen presented complex variant translocations, involving chromosomes 9 and 22 plus a third chromosome (12 patients) or a fourth chromosome as well (1 patient). The chromosomes involved in the rearrangements were: 2q21, 2q11, 3q21, 4q31, 4q31, 5q14, 5q31, 7p15, 9q22, 11q13, 13q11, 17q25, 20p11, and Yq11. In 6/18 patients, the rearrangements had not been previously reported in CML. Five patients (27.7%) presented ACAs: duplication of the Ph chromosome, monosomy 7, add(21)(q22), inv(11)(p13q23), and t(4;16)(p16;q12). Two patients with ACAs developed blast crisis: one at diagnosis, who underwent allogeneic transplantation and the second patient ten months after diagnosis died. One other patient developed ACAs 15 years after diagnosis with blast crisis (acute lymphoblastic leukemia) and died. Seven of the 18 patients had the b2a2 transcript, 10 had b3a2, and 1 had b3a3. Of the 15 patients with continuous follow-up data, 13 are alive. Data for molecular follow-up is available for 12 patients: 10 achieved deep molecular response (MR4, MR4.5) (83%) with a median time to achievement of 17.4 months (range 2-96 months), one achieved MMR (8%), and the other has <MMR (8%), with a median follow-up time of 99.7 months (range 17.1-345.6 months). Median time to achieve ≥MMR was 7.5 months (range 2-17 months). Ten patients had cytogenetic follow-up, of whom 9 (90%) achieved complete cytogenetic response (CCyR). Median time to CCyR for patients who received TKI frontline, was 6 months (range 2-22 months).

CONCLUSION: The presence of Ph chromosome variants does not appear to be associated with a distinct disease phenotype; however, the prognostic significance of each individual variant should be clarified. In the present study, the patient with the translocation t(3;9;22)(q21;q34;q11), add(21)(q22) rapidly developed blast crisis and died, a finding consistent with the adverse prognosis of this particular variant as reported in the literature. Conventional karyotype is the only appropriate method for identifying any variant of the Philadelphia chromosome.

P28. MACROCYTIC ANEMIA AND ELEVATED VITAMIN B12 AS CLUES TO SYSTEMIC MASTOCYTOSIS WITH AN ASSOCIATED MYELODYSPLASTIC SYNDROME

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OBJECTIVE: Systemic mastocytosis with an associated hematologic neoplasm (SM-AHN) is an advanced form of systemic mastocytosis in which two clonal hematologic disorders coexist, posing diagnostic, prognostic, and therapeutic challenges. Macrocytic anemia with megaloblastoid marrow features may mimic vitamin B12-deficiency anemia, whereas paradoxically elevated serum vitamin B12 can be a clue to an underlying myeloid neoplasm. We report a case of systemic mastocytosis with an associated myelodysplastic syndrome (SM-MDS), identified during investigation of otherwise unexplained macrocytic anemia, thrombocytopenia, and markedly elevated vitamin B12.

METHODS: A 67-year-old woman, incidentally under evaluation for a persistent dry cough with an unremarkable chest CT apart from an old T11 osteoporotic fracture, was found to have macrocytic anemia (Hb 10.6-11.2 g/dL, MCV 96-97 fL), mild thrombocytopenia (87-119×10^3/μL), and serum vitamin B12 >1500 pg/mL. Other causes of macrocytosis and marrow dysplasia were excluded. The combination of unexplained cytopenias, macrocytosis, and elevated vitamin B12 prompted bone marrow evaluation with immunophenotypic, cytogenetic, and molecular testing.

RESULTS: Bone marrow examination showed increased cellularity and erythroid hyperplasia with dyserythropoietic/megaloblastoid features involving >10% of erythroid precursors, ~4% CD34+ progenitors, and a normal karyotype (46, XX). NGS (51-gene myeloid panel) identified SF3B1 K700E (VAF 40.4%) and a RUNX1 p.(Gly168_Gly170dup) variant of uncertain significance, with no TP53 mutations detected, establishing a diagnosis of myelodysplastic neoplasm with low blasts and SF3B1 mutation (WHO 2022), classified as low risk by both IPSS-R and IPSS-M. In parallel, a ~10% infiltrate of round-to-spindle-shaped mast cells forming dense multifocal aggregates (>15 cells/aggregate) expressed CD117, tryptase, CD25 and CD30; serum tryptase was markedly elevated (77.7 ng/mL; peak 115 ng/mL); and KIT D816V was detected by NGS (VAF 23.1%) and confirmed by high-sensitivity peripheral-blood PCR (VAF 26%), establishing systemic mastocytosis. Low-dose whole-body CT revealed, beyond the known T11 fracture, two additional fractures and mandibular osteolysis, indicating advanced disease with skeletal involvement. Avapritinib was initiated together with H1/H2 blockade and self-injectable epinephrine. Follow-up will include serial serum tryptase and high-sensitivity KIT D816V VAF monitoring; HLA typing of the patient and her three siblings is underway, with planned referral to a transplant center for individualized assessment.

CONCLUSION: This case highlights that systemic mastocytosis should be considered not only in patients with anaphylactic or other mediator-related manifestations, but also in those with unexplained cytopenias and skeletal manifestations, including osteoporosis, fragility fractures, or osteolytic lesions. In SM-AHN, diagnosis requires integration of morphologic, immunophenotypic, and molecular findings across both clonal components, and risk assessment should not rely on the conventional risk classification of the associated neoplasm alone, since apparently favorable MDS features do not necessarily translate into an indolent overall course. In this context, early consideration of allogeneic transplant evaluation may be warranted even when the associated MDS is classified as low risk, pending individualized assessment of both disease components. Comprehensive molecular characterization, KIT-directed therapy where indicated, and multidisciplinary evaluation are central to individualized management.

P29. HOW REPRESENTATIVE WAS AZA-001? A REAL-WORLD EVALUATION OF AZACITIDINE OUTCOMES ACCORDING TO ELIGIBILITY FOR THE PIVOTAL REGISTRATION TRIAL. A REPORT FROM THE HELLENIC MDS STUDY GROUP

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OBJECTIVE: Background: The AZA-001 trial established azacitidine as the standard first-line treatment for patients with higher-risk myelodysplastic neoplasms (MDS). However, the study population was highly selected, raising questions about how well its findings apply to patients treated in routine practice. The aim of the current study was to compare progression-free survival (PFS) and overall survival (OS) among patients who did and did not meet the eligibility criteria of the pivotal AZA-001 trial.

METHODS: This retrospective cohort study included 1,141 patients with MDS treated with azacitidine from a multicenter national registry. Patients were classified according to whether they met the AZA-001 inclusion and exclusion criteria. The primary endpoints were PFS and OS. Multivariable Cox proportional hazards regression was used to examine the association between trial eligibility and survival outcomes after adjustment for established prognostic factors. Variables retained in the final models were selected using backward elimination (retention criterion $p<0.05$).

P29. (continue)

RESULTS: Results: Of the 1,141 patients, only 177 (15.5%) met the AZA-001 eligibility criteria, while 964 (84.5%) would have been excluded from the pivotal trial. Among patients who met the eligibility criteria, the median age was 72.3 years (range, 50-86.5), and 115 (65%) were female. All patients had high-risk primary MDS. The mean lactate dehydrogenase (LDH) value at diagnosis was 270 ±161 U/L (normal value <225 U/L), and the majority had an ECOG performance status of 0 (n=103, 58.2%). The median time from diagnosis to treatment initiation was 1.2 months (IQR, 0 - 35.4), and the median number of azacitidine cycles received was 9 (IQR, 1 - 52). The complete PFS analysis included 1,017 patients with 717 progression or death events, and the OS analysis included 1,047 patients with 661 deaths. After adjustment for baseline prognostic factors, meeting the AZA-001 eligibility criteria was independently associated with improved PFS (hazard ratio [HR]=0.68, 95% confidence interval [CI]=0.54-0.86; p=0.001) and OS (HR=0.68, 95%CI:0.52-0.87; p=0.003). Poorer ECOG performance status, elevated LDH, and higher IPSS-R risk group were independently associated with worse PFS and OS. Red blood cell transfusion dependence and older age were associated with inferior OS.

CONCLUSION: Conclusions: Only one in six patients treated with azacitidine in routine clinical practice met the eligibility criteria of the landmark AZA-001 trial, highlighting the limited generalizability of the pivotal study population. Patients who met the AZA-001 eligibility criteria experienced significantly longer PFS and OS after adjustment for established prognostic factors. These findings suggest that the outcomes reported in AZA-001 may not fully reflect those achieved in the broader population of patients treated in routine practice and emphasize the complementary role of real-world evidence in evaluating the effectiveness of anticancer therapies outside the clinical trial setting. Consistent with our findings, previous real-world studies have confirmed azacitidine's survival benefit, though more modestly than the one reported in AZA-001.

P30. REAL-WORLD DATA OF CMV REACTIVATION IN PATIENTS RECEIVING BISPECIFIC ANTIBODIES

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OBJECTIVE: Bispecific-antibodies (BsAbs) have emerged as an effective treatment option for patients with relapsed-refractory hematologic malignancies. However, prolonged T-cell activation and immune dysregulation increase the risk of opportunistic infections, including cytomegalovirus (CMV)-reactivation. Data regarding the incidence, risk factors, clinical course, and outcomes of CMV-reactivation in patients treated with BsAbs remain limited. Thus, we aim to evaluate the incidence, timing, risk factors, management, and clinical outcomes of CMV-reactivation in patients receiving BsAb-therapy in a real-world clinical setting.

METHODS: We conducted a retrospective observational study of consecutive adult patients who received BsAb-therapy for hematologic malignancies at our institution between 2022 and 2026. Demographic characteristics, disease-related variables, prior lines of therapy, previous hematopoietic stem cell transplantation, corticosteroid exposure, occurrence of cytokine release syndrome, CMV-monitoring practices, antiviral treatment, and clinical outcomes were collected from electronic medical records. We performed routine CMV-surveillance by quantitative polymerase chain reaction and defined CMV-reactivation as detectable CMV-DNAemia according to institutional criteria. The primary endpoint was the incidence of CMV-reactivation. Secondary endpoints included time to reactivation, identification of risk factors, requirement for antiviral therapy, interruption of BsAb-treatment, recurrent CMV infection, and overall survival.

RESULTS: A total of 23 patients receiving BsAb-therapy were included. Median age was 65 years (33-79), and 48% were male. The underlying diagnosis was multiple myeloma in 61% and other hematologic malignancies in 39%. Patients had received a median of 4 prior lines of therapy, while 76% had undergone prior autologous hematopoietic stem-cell transplantation. All patients with multiple myeloma received regular IVIG supplementation. CMV-reactivation occurred in 6 patients (26%), with a median time of 85 days since BsAb initiation. The median peak CMV-viral load was 7.5x10^3 IU/mL. Symptomatic CMV-disease developed in 4 (17%), whereas 2 patients (7%) had asymptomatic CMV-DNAemia. Factors associated with CMV-reactivation trend included cumulative corticosteroid exposure (60 vs 48 mg dexamethasone equivalent, P=0.7), grade ≥2 cytokine release syndrome (35 vs 18%, P=0.6) and median number of tocilizumab doses required 3 vs 2, P=0.7. However, in multivariable analysis, no factor remained independently associated with CMV-reactivation. Preemptive antiviral therapy was initiated in all patients with CMV-DNAemia. The median CMV-viral load at treatment initiation was 7.5x10^3 IU/mL. The most frequently used antiviral agent was valganciclovir (50%), followed by ganciclovir (34%) and maribavir (16%). Among patients receiving preemptive treatment, CMV-DNAemia resolved in all patients after a median of 15 days. Progression to clinically significant CMV-disease despite preemptive therapy did not occur. Temporary interruption of BsAb-therapy was required in all patients, and CMV-reactivation was observed in 1 patient. OS at 12-months was 80% in patients with CMV-reactivation vs 93% in those without reactivation (P=0.9)

P30. (continue)

CONCLUSION: CMV-reactivation was a relatively frequent complication in patients receiving BsAb therapy for hematologic malignancies in this real-world cohort. Routine molecular surveillance enabled early detection of CMV-DNAemia, allowing preemptive antiviral treatment in most cases and limiting progression to clinically significant CMV-disease. Nevertheless, CMV-reactivation led to treatment interruptions in a subset of patients. These findings support risk-adapted CMV-monitoring and preemptive treatment strategies in patients receiving BsAbs and highlight the need for prospective studies to define optimal prophylaxis, surveillance and management approaches.

P31. PRESUMED INVASIVE FUNGAL SINO-ORBITAL DISEASE COMPLICATED BY INTERNAL CAROTID ARTERY ANEURYSM RUPTURE IN HAIRY CELL LEUKEMIA

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OBJECTIVE: To describe a rare, life-threatening vascular complication of presumed invasive fungal sino-orbital-cavernous disease in a patient with hairy cell leukemia (HCL) receiving pentostatin, culminating in internal carotid artery (ICA) aneurysm rupture and subarachnoid hemorrhage (SAH) despite persistently negative microbiological investigations.

METHODS: We report a 56-year-old man with newly diagnosed HCL who developed prolonged febrile neutropenia shortly after initiation of pentostatin. Diagnostic evaluation included serial cranial and orbital CT and MRI with arterial and venous angiographic sequences, cerebrospinal fluid analysis with extensive molecular pathogen testing, serum and CSF fungal biomarkers, and endoscopic sinus surgery with intraoperative microbiological sampling.

RESULTS: During hospitalization, the patient developed progressive left ophthalmoplegia and visual loss. Imaging demonstrated an invasive process involving the left sphenoid sinus, optic nerve, and cavernous sinus, together with thrombosis of the torcular Herophili. Emergency endoscopic sphenoidectomy drained purulent material; however, cultures, broad molecular pathogen panels, and fungal sequencing remained negative. A single transiently positive β-D-glucan, together with the clinical and radiological findings, supported presumed invasive fungal disease, and broad-spectrum antimicrobial and mold-active antifungal treatment was administered. Despite treatment, ophthalmoplegia progressed to amaurosis. Follow-up vascular imaging revealed two newly developed left ICA aneurysms, one cavernous fusiform and one supraclinoid saccular. The supraclinoid aneurysm subsequently ruptured, causing SAH while the patient was receiving anticoagulation for venous sinus thrombosis. He presented with GCS 6/15, focal seizures, expressive aphasia, and right hemiparesis. Emergency endovascular ICA occlusion with coil embolization achieved complete exclusion of the ruptured aneurysm without procedural complications. Antimicrobial therapy was subsequently de-escalated to isavuconazole monotherapy. At discharge, the patient was afebrile, hemodynamically stable, ambulatory, and GCS 15/15. At two-month follow-up, aneurysm occlusion remained stable, with near-complete recovery of ocular motility and eyelid function, although optic nerve atrophy persisted.

CONCLUSION: Presumed invasive fungal sino-orbital-cavernous disease in profoundly immunocompromised patients may cause both venous thrombosis and destructive arterial complications despite negative microbiological investigations. The coexistence of venous thrombosis and occult mycotic aneurysms poses a particularly challenging balance between thrombotic and hemorrhagic risk. This case supports a high index of suspicion based on clinical and radiological findings, consideration of serial arterial and venous vascular imaging in progressive sino-cavernous disease, and early multidisciplinary involvement. Timely endovascular intervention can be lifesaving even after aneurysmal rupture and severe neurological deterioration.

P32. INVESTIGATING THE ROLE OF COMPLEMENT RECEPTOR 1 (CR1) AS A NOVEL BIOMARKER FOR RECURRENT IMMUNOTHROMBOSIS IN ANTIPHOSPHOLIPID SYNDROME

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OBJECTIVE: Antiphospholipid Syndrome (APS) is a crucial systemic autoimmune disorder characterized by thrombotic and/or obstetric events occurring in patients with persistent antiphospholipid antibodies (aPL). It is also known that Complement Receptor 1 (CR1) normally regulates the complement system by binding to C4b and C3b components, playing a key role in the clearance of soluble immune-complexes. Recent studies have shown that low levels of CR1 expression make it as the key driver for the development of catastrophic APS. Considering that the available data on CR1 expression in APS are limited, this study aims to provide a preliminary assessment of CR1 expression in specific cell populations and to investigate possible associations with clinical characteristics.

METHODS: This cross-sectional study included adult patients who met the 2023 ACR/EULAR classification criteria for primary APS. Specific aPL were quantified, such as: lupus anticoagulant, anti-cardiolipin IgM/IgG and anti-β2-glycoprotein I (anti-β2GPI) IgA/IgM/IgG. CR1 expression was dissected in erythrocytes, granulocytes, monocytes and lymphocytes using flow cytometry, both as an absolute percentage (CR1-positive cells) and as Mean Fluorescence Intensity (MFI).

P32. (continue)

RESULTS: We studied 28 patients with APS, with a median age at diagnosis of 50 years [interquartile range 43-58] and a median disease duration at study enrollment of 4 years (2.5-10.5). Fifteen participants (53.6%) were female (Table 1). Nine patients (32.1%) had isolated venous thrombosis, 10 (35.7%) isolated arterial thrombosis, and 9 (32.1%) recurrent venous thrombosis. The median number of thrombotic episodes was 1 (1-2). Among the 27 patients with an available aPL profile, 22 (81.5%) were LA-positive and 13 (48.1%) had triple positivity. Patients with recurrent events had higher CR1 expression (MFI) in granulocytes than those with a history of a single thrombotic event (n=19) [73.0±38.4 vs 38.5±21.0, p=0.029]. Furthermore, LA-positive patients (n=22), compared with LA-negative patients (n=5), had elevated expression levels of CR1 in lymphocytes [4.2 (3.5-6.3) vs 2.6 (2.6-3.2), p=0.039] and a higher percentage of CR1-positive lymphocytes [27.2% (9.3) vs 17.5% (2.8), p<0.001]. Patients with anti-β2GPI IgG positivity exhibited a lower percentage of CR1-positive erythrocytes (39.1% vs 54.1%, p=0.023), whereas those with ACA IgM-positivity had a higher percentage of CR1-positive monocytes (98.1% versus 91.2%, p=0.012). Furthermore, patients with ACA IgG positivity had lower CR1 expression on erythrocytes (6.0 vs 8.0, p=0.036) and a lower percentage of CR1-positive erythrocytes (40.5% vs 54.1%, p=0.040). In univariate analysis, CR1 expression in granulocytes was positively correlated with the number of thrombotic events (r=0.447, p = 0.017), whereas in lymphocytes was negatively correlated with age at diagnosis (r = –0.448, p = 0.019). Moreover, the percentages of CR1-positive monocytes and lymphocytes were negatively correlated with disease duration (r = –0.613, p < 0.001) and age at diagnosis (r = –0.54, p = 0.003), respectively.

CONCLUSION: This study revealed significant findings regarding the role of CR1 as a critical biomarker of thrombotic recurrence in APS. However, due to the small sample size, validation is required in larger prospective studies, as well as correlations with other markers of thomboinflammation, complement activation and endothelial injury, to further elucidate the role of CR1 in the immunopathogenesis of APS.

P33. CORRELATION OF PLATELET INDICES WITH RED BLOOD CELL PARAMETERS IN SYSTEMIC INFLAMMATION AND NEOPLASIA

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OBJECTIVE: Systemic inflammatory responses and neoplastic processes affect bone marrow hematopoiesis through the action of pro-inflammatory cytokines (such as IL-6, TNF-\alpha, and IL-1), inducing alterations in both erythropoiesis and megakaryopoiesis. The aim of this study was to evaluate the potential association between platelet indices —specifically Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), and Platelet Large Cell Ratio (P-LCR)— and red blood cell parameters, namely Hemoglobin (Hb), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), and Red Cell Distribution Width (RDW), and to assess combined ratios (MPV/MCV, PDW/RDW) as accessible biomarkers of disease severity and activity.
METHODS: A total of 1,110 peripheral blood samples were obtained from outpatients visiting four major Greek Hospitals and analyzed on Sysmex XN-2000 automated hematology analyzers. One thousand and seven (1,007) samples were obtained from patients with various systemic inflammatory (N = 524) and neoplastic disorders (N = 483), including 50 pregnant women, and 103 samples from healthy controls. Normality testing, correlation analyses (Pearson r / Spearman rho), and comparative ANOVA (with Bonferroni post-hoc correction) were conducted between parameters across both lineages.
RESULTS: Among the 1,007 patients, anemia (Hb < 12 g/dL for men and Hb< 11.5\g/dL for women) was identified in 430 patients (42.7%) (215 men and 215 women). Reactive or secondary thrombocytosis (PLT > 400 10^3/muL) was documented in 186 patients (18.5%). Patients demonstrated a statistically significant negative correlation between Hb levels and MPV ($r = -0.34$, $p < 0.001$) as well as PDW ($r = -0.39$, $p < 0.001$), reflecting inflammatory suppression of erythropoiesis alongside compensatory stimulation of megakaryopoiesis. Furthermore, a strong positive correlation was observed between RDW and PDW ($r = 0.45$, $p < 0.001$), indicating common factors inducing combined anisocytosis and anisothrombocytosis. Evaluation of erythrocytic indices against platelet volume showed a weak, non-statistically significant positive trend between MCV and MPV ($r = 0.026$, $p = 0.791$) as well as MCH and MPV ($r = 0.034$, $p = 0.723$). Assessment of platelet indices against total platelet count revealed a statistically significant negative correlation for MPV vs PLT ($r = -0.325$, $p = 0.001$) and PDW vs PLT ($r = -0.226$, $p = 0.018$), whereas P-LCR vs PLT showed a weak negative correlation ($r = -0.178$, $p = 0.215$).
CONCLUSION: Co-evaluation of platelet indices and red blood cell parameters provides a comprehensive view of the impact of systemic inflammation and neoplasia on bone marrow hematopoiesis. Combined ratios (such as MPV/MCV and PDW/RDW), as previously proposed in clinical literature to assess inflammatory burden and thrombotic risk, constitute highly accessible, cost-effective, and sensitive biomarkers that enhance the diagnostic and prognostic utility of routine complete blood counts.

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