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

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Sp07

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

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Allogeneic transplantation (HSCT) is an effective curative therapy for high risk acute myeloid leukemia (AML) which account for 38% of the transplants in Europe (1). Prior to HSCT, a conditioning or preparative regimen is administered. The conditioning regimen has 2 components; one target the myeloid system aiming in eradication of the leukemic clones, while the other target the immune/lymphoid system to ensure engraftment and to prevent rejection. Some of the compounds used in the conditioning are more myeloablative in nature for example busulfan or melphalan) 2-4) while others are more lymphodepliting like fludarabine or Cytoxan (5). Traditionally, the pre HSCT conditioning was myeloablative (MAC) and includes total body irradiation (TBI) in combination with cyclophosphamide (CY) (2-3). High-dose busulfan (Bu) is the most commonly used TBI-free-based myeloablative conditioning (2-3). In HSCT from unrelated or mismatched donors the pre transplantation conditioning typically includes serotherapy with anti-thymocyte globulin (ATG) or the CAMPATH monoclonal antibody in order to avoid rejection and ensure engraftment while preventing graft versus host disease (GVHD) (5). However, the MAC is typically associated with significant morbidity and mortality due to the toxicity of the preparative regimen, GVHD, and the immune-deficient state that accompanies the procedure (2,5-6). This is especially true in patients above the age 55-60 years old and in patients with comorbidities which are the majority of AML patients. Extensive research, including pharmacokinetic and pharmacodynamics studies has been directed therefore towards the development of safer and less toxic conditioning regimens for HSCT, optimizing the conditioning allowing its applications to elderly patients and patients with comorbidities (2,5-6). These modern conditioning regimens which are based in part on the immune-mediated graft versus leukemia (GVL) effect are in principle low-dose, less toxic and tolerable conditioning regimens termed reduced intensity (RIC) with different immunosuppressive and myelosuppressive properties (5-7). These regimens combine immunosuppressive agents (such as fludarabine with or without serotherapy or targeted therapy with agents with moderate myelosuppressive effects or novel agents. However, they typically result in higher relapse rate especially in patients undergoing HSCT while not in remission and in patients with high risk leukemia including patients with adverse cytogenetics, high risk mutations and patients with positive measurable residual disease (MRD) at time of transplants. The optimal regimen is thus the one with intensive anti-leukemic activity, but with limited toxicity-the so called reduced toxicity regiments (RTC). These novel regimens are mostly fludarabine based and incorporate drugs like melphalan; thiotepa; treosulfan and clofarabine (8-11). Other protocols are the so called TBF protocol that include two alkylating agents like busulfan and thiotepa(9,11) and the FLAMSA protocol that includes fludarabine, cytarabine, and amsacrine (11).The RIC and RTC regimens enable HSCT in elderly patients and those with comorbidities reducing drastically transplant related mortality and organ toxicities in combination with improved anti leukemic effect. Efficient safe pre transplant conditioning protocols are continuing to be developed. Future protocols will most probably incorporate specific anti leukemic targeted novel compounds as well as monoclonal and radiolabeled antibodies.

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Sp08

LESSONS FROM THE EUROPEAN AND ISRAEL NATIONAL MDS REGISTRY

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

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

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Sp09

EMERGING DATA FOR CANCER ASSOCIATED THROMBOSIS TREATMENT

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

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Sp10

VASCULAR DISEASES IN PNH

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