between pts with MM and RI regardless of renal function. The aim of the DARE study [NCT03450057] was to assess the safety and efficacy of DARA in pts with RRMM and severe RI or requiring hemodialysis.

Methodology: DARE is a prospective, open-label, multicenter, phase 2 study, which included pts with documented RRMM and severe RI (eGFR < 30 ml/min/1.73m^2) or requiring hemodialysis. Participating pts must have ≥2 lines of therapy with both bortezomib- and lenalidomide-based regimens and an Eastern Cooperative Oncology Group performance status (ECOG PS) score ≤2. Exclusion criteria include previous DARA or other anti-CD38 therapy exposure. Pts receive 28-day treatment cycles with 16 mg/kg intravenous DARA (weekly for cycles 1–2, every 2 weeks [wks] for cycles 3–6, and every 4 wks thereafter) and oral dexamethasone (40 mg weekly, each cycle). The primary endpoint is progression-free survival (PFS). Secondary endpoints are overall response rate (ORR; proportion of pts with partial response or better), renal response rate (RRR; proportion of pts with best response of renal partial response or better), and safety. All responses are based on investigators' assessment per International Myeloma Working Group criteria.

Results: Thirty-eight pts with obtained informed consent, enrolled in 7 centers, were included in this analysis. The pts median age was 72 years, and most were male (75%). At study initiation 7% and 93% of pts had International Staging System (ISS) stage II and III disease, respectively; 51% and 49% of pts had revised ISS stage II and III, respectively. At baseline, the median time from MM diagnosis was 4.2 years; 24%, 72%, and 4% pts had ECOG PS 0, 1, and 2, respectively; the median eGFR was 13.0 mL/min/1.73 m^2. Median number of prior lines of therapy was 3, and 35% pts had previous autologous stem cell transplantation. The median number of therapy cycles received per patient was 7.0. The median follow-up was 8 months and the 6-month PFS rate was 51%. The ORR was 41% (including VGPR in 29% of pts). The RRR was 22%. The median time from first DARA dose to first partial response or better was 1.5 months. Of all grade 3 or 4 AEs, the most frequent were anemia (21%), thrombocytopenia (13%), hyperkalemia (11%), and hyperglycemia (8%).

Conclusion: DARA plus dexamethasone was efficacious with a favorable safety profile in pts with RRMM and severe RI or requiring dialysis. Hematologic responses were high in these heavily pretreated pts, while more than one-fifth of them also achieved a renal response.

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OP 12

A novel microrna signature with clinical significance in multiple myeloma

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Objective: MicroRNAs (miRNA) are single-stranded, small non-coding RNA molecules (~21 nucleotides) that regulate protein-coding gene expression at the post-transcriptional level, mainly through interactions with the 3′-untranslated region of target mRNAs. Such interactions lead to mRNA degradation and/or translational repression, depending on the complementarity of the miRNA seed sequence with the mRNAs 3′-untranslated region. They can function as oncogenes or tumor suppressors, possessing a vital role in all stages of tumorigenesis and cancer progression. In the present study, we have investigated the clinical significance of a molecular signature consisting of 10 cancer-related miRNAs in multiple myeloma (MM): miR-15a, miR-16, miR-21, miR-221, miR-222, miR-25, miR-125, miR-155, miR-223, and miR-181a. These molecules were selected due to their well-documented role and clinical significance in numerous human malignancies.

Methodology: Bone marrow aspiration samples were collected from 94 patients with multiple myeloma (MM) and smoldering multiple myeloma (sMM) at the time of diagnosis and CD138+ plasma cells were positively selected using magnetic beads coated with an anti-CD138 antibody. Total RNA was isolated using TRIZol, 200ng RNA of each sample were polyadenylated at the 3′ end and reversely transcribed. An in-house developed real-time quantitative PCR assay was conducted and the results were biostatistically analyzed. For the normalization of the expression levels of each miRNA, the mean expression of two small nucleolar RNAs (RNU43 and RNU48) was used as reference.

Results: Seventy-six out of the 94 BM aspiration samples were derived from MM patients and 18 from sMM patients. The MM patients were classified, according to the R-ISS staging system, as follows: 15 patients with stage I disease, 42 patients with stage II, and 19 patients with stage III. Forty-nine myeloma patients presented with osteolytic lesions at diagnosis. The statistical analysis revealed significantly lower expression levels of miR-16 ($p = 0.036$) and miR-155 ($p = 0.045$) in CD138+ cells of MM patients, compared to those from sMM patients. Furthermore, miR-221 and miR-222 expression levels were negatively correlated with R-ISS; thus, miR-221 and miR-222 expression was significantly downregulated in MM patients with R-ISS stage III ($p = 0.004$ and 0.034, respectively). Interestingly, the expression levels of miR-15a ($p = 0.048$) and miR-16 ($p = 0.047$) were decreased in

MM patients with osteolytic lesions at the time of diagnosis, compared to those without osteolyses.

Conclusion: We conclude that miR-221/222 cluster correlates with more favorable R-ISS stage, revealing a potential favorable prognostic value in MM patients. MiR-15a and miR-16 correlate with the presence of osteolytic disease in MM. The observed decreased expression of these two miRNAs in symptomatic MM patients with osteolytic lesions could constitute a possible biomarker for the occurrence of bone disease. Moreover, decreased expression of miR-16 and miR-155 in MM patients, compared to sMM patients may indicate a putative predictive biomarker able to distinguish symptomatic patients from sMM patients. This ongoing study will further reveal the possible prognostic significance of this 10 miRNAs signature studied, when response to therapy, progression-free and overall survival is available.

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OP 13

Peripheral blood immune profiling of multiple myeloma patients at diagnosis: correlations with circulating plasma cells

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Objective: Circulating Tumor Plasma Cells (CTPCs) detected in the peripheral blood (PB) of newly diagnosed Multiple Myeloma (MM) patients have been associated with adverse prognostic features and poor overall survival. The correlation of CTPCs with the immune profile in PB remains unknown. The aim of the present study was to evaluate the immune profile in the PB of patients with newly diagnosed MM and correlate the results with the presence of low or high number of CTPCs.

Methodology: We analyzed myeloid-derived suppressor cells (MDSCs) and major immune T cell subpopulations, including regulatory T cells (Tregs), in the PB of newly diagnosed MM patients. The percentages of MDCSs and Tregs were correlated with the concomitant presence of low (<0.003%) or high (>0.05%) CTPCs. PB samples of 26 newly diagnosed MM patients were analyzed with flow cytometry using the following panels: (a) the minimal residual disease EuroFlow-based next-generation flow cytometry (NGF) panel, for the detection and identification of PB CTPCs; (b) a panel comprising the surface markers CD15, HLA-DR, CD14, CD124, CD33, CD11b, and LinCD56-CD3-CD19, for the detection of polymorphonuclear MDSCs (PMN-MDSCs), monocytic MDSCs (M-MDSCs) and early-stage MDSCs (eMDSCs); and c) two panels comprising the surface and intra-cellular markers CD25, CD3, CD39, CTLA-4, CD4, CD8, CD45RO, CD45RA, HLA-DR, CD127, Ki67, and FoxP3, for the detection of CD4, CD8 T cells and Tregs. For the evaluation of (b) and (c), prior to staining, mononuclear cells (PBMCs) were isolated from PB using density-gradient centrifugation on Ficoll-paque.

Results: Using NGF, 12 MM patients had high and 14 low CTPCs in their PB. MDSCs averaged $5.42 \pm 5.9\%$ of PBMCs, whereas PMN-MDSCs were the most abundant subpopulation ($4.38 \pm 5.7\%$ of PBMCs) and displayed great heterogeneity between patients. Additionally, 22 distinct T subpopulations were phenotypically identified and analyzed, including CD4 and CD8 T cells, naive Tregs (CD45RA+), effector Tregs (CD45RO+), terminal effectors (HLADR+), CD39+ suppressor Tregs, CD8 Tregs and their proliferating (Ki67+) counterparts. Comparing the percentages of the immune populations among patients with high versus low CTPCs, M-MDSCs were significantly more abundant ($p < 0.05$) in patients with low CTPCs, whereas immune profiling of T cells revealed (although not reaching statistical significance) the presence of increased percentages of proliferating Tregs in those with low CTPCs and increased percentages of naïve CD4 T cells in patients with high CTPCs.

Conclusion: To our knowledge, this is the first study correlating the presence of high versus low CTPCs with the immune profile in PB of MM patients. Low CTPCs correlated with the presence of higher percentage of M-MDSCs. Since the latter has been associated with the CCR5-dependent recruitment of Tregs into the tumor site, our findings suggest that, in low CTPC MM patients, a more effective immune surveillance mechanism, mediated by the interaction of M-MDSCs – Tregs, likely controls CTPC expansion and may contribute to a more favorable prognosis. Analysis of more samples, which is ongoing, will validate our findings and provide more solid results.

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OTHER DISEASES

OP 14

COVID-19 infection in cancer patients: a systematic review and meta-analysis with emphasizing the risk and prognosis stratification

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Objective: Various cancer societies worldwide have released guidelines to care for cancer patients suffering from COVID-19. Given the findings from our meta-analysis, in the absence of prospective data, we recommend diligent preventive care measures, full supportive care for immunosuppressed patients to minimize the risk of infection, limiting patient's visits to the hospital when possible and using telecommunication technology. Future studies should focus on collecting all the baseline characteristics of cancer patients suffering from COVID-19, all cancer and chemotherapy or radiation-related variables as well as the detailed COVID-19 care protocol followed in these patients and the dynamic biochemical and inflammatory profile of these patients during the infection.