Conclusion: Sarcopenia after 2 cycles of chemotherapy may be a risk factor for BPT. All patients with sarcopenia received same dose of bleomycin in this study. A significant relation between loss of muscle mass and BPT indicates that higher bleomycin doses in accordance with muscle mass may be a risk factor for BPT development. Dose reductions according to muscle mass can be more logical even if the BMI status of the patients remains the same after 2 cycles of chemotherapy. Randomized clinical trials are needed in this very important topic.

https://doi.org/10.1016/j.htct.2020.09.041

MYELOMA

OP 10

Bendamustine-bortezomib-dexamethasone (BVD) in heavily pretreated multiple myeloma: old/new in novel agents' era

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Objective: Bendamustine is an old bi-functional alkylating agent which has proved to be effective in relapsed, refractory and in new diagnosed Multiple Myeloma (MM).

Case report: Thus, aiming to provide further insights in this field, also in novel agents' era, we present here a retrospective, real-life analysis of patients with relapsed/refractory MM (rrMM), who had received salvage therapy with bendamustine in combination with bortezomib and dexamethasone (BVD).

Methodology: 81 patients (44 M/37 F), with rrMM, median age at diagnosis 59.4 years (r. 36–82), median age at start of treatment 63.6 years (r.37–86) treated with several lines of treatments (median 6, r. 2–11), every refractory to all the drugs previously received (also Bortezomib), received BVD (B 90 mg/sqm days 1,2; V 1.3 mg/sqm days 1,4,8,11, D 20 mg days 1,2,4,5,8,9,11,12, Pegfilgrastim day +4) every 28 days, until progression. All patients had previously received bortezomib-based and IMIDs-based treatments, and 32% (26/81) had also received radiotherapy. 69% (56/81) had undergone single or double autologous and three (2%) allogeneic stem cell transplant. All patients were relapsed and refractory to last therapies received before BVD.

Results: Bendamustine was well tolerated, with grade 3–4 transfusion-dependent anemia in 56% (46/81) of patients, and 43% (35/81) grade 3–4 neutropenia (no ospedalization was required, no septic shocks were observed). No severe extrahematologic toxicity was observed, only grade 1 gastrointestinal side effect (nausea), treated by common antiemetic drugs. According to IMWG, ORR was 63% (51/81: 7 CR, 18 VGPR, 15 PR, 11 MR) with 11 PD and 19 patients in SD, which can be considered as an impressive result in this subset of rrMM patients. In particular, for 11 patients, BVD was, after having achieved at least a PR, a bridge to second auSCT, and for two patients a bridge to alloSCT. Eight patients have surprisingly achieved a notable PR after failure of novel agents (i.e. Carfilzomib, Daratumumab and Pomalidomide). Median time to response was 1.3 months (r.1–3), median OS from diagnosis was 67.3 months (r.6–151), median OS from start of Bendamustine was 9.6 months (r.2–36).

Conclusion: The triplet Bendamustine-Bortezomib-Dexamethasone has shown significant efficacy in a particularly severe setting of patients, relapsed and refractory to all available therapeutic resources, and, in particular cases, it could be considered as a bridge to a second autologous or allogenic SCT, also after failure of novel agents.

https://doi.org/10.1016/j.htct.2020.09.042

OP 11

Efficacy and safety of daratumumab with dexamethasone in patients with relapsed/refractory multiple myeloma and severe renal impairment: results of the phase 2 dare study

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Objective: Patients (pts) with multiple myeloma (MM) and severe renal impairment (RI) have poorer overall survival. Daratumumab (DARA), an IgG1κ human monoclonal antibody that targets CD38, has shown efficacy and a favorable safety profile in pts with relapsed or refractory MM (RRMM). Moreover, in population pharmacokinetic analyses, no clinically important differences in exposure to DARA were observed

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.

https://doi.org/10.1016/j.htct.2020.09.043

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