2. NEWLY DIAGNOSED MULTIPLE MYELOMA

DARA-VTD AND ASCT+ LENALIDOMIDE LED TO HIGH COMPLETE REIMISSION AND MINIMAL RESIDUAL DISEASE NEGATIVITY RATES BY NGF: A REAL-WORLD STUDY OF THE TUSCAN MYELOMA NETWORK IN 228 PATIENTS

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Background. The CASSIOPEIA phase 3 study compared two groups of MM patients eligible for autologous transplantation (TE) by adding the monoclonal antibody daratumumab to standard induction therapy (VTD), consolidation and maintenance for 2 years compared to observation. The study demonstrated a deeper rate of response in the daratumumab group in terms of responses (>CR 23%) , minimal residual disease (MRD) negativity (64% post ASCT) and in terms of survivals compared to the VTD-induced group. Real-life "DARA-VTD" by the Multiple Myeloma Tuscan network (RTM) is an observational and retrospective, multicenter, non-commercial (no-profit) clinical study that tested real-life data in patients with multiple myeloma eligible for ASCT treated according to the DaraVTd induction regimen, ASCT, consolidation, and lenalidomide maintenance (as Daratumumab was not allowed), deriving from the experience of 7 centers.

Methods. MM patients TE subsequently presented to the centers received treatment with subcutaneous Dara-VTD as per label. After 4 cycles of therapy, CSE collection was performed after mobilization with G-CSF alone or with Cyclophosphamide, adding Plerixafor administration in case of failure of the procedure at the first attempt. Following the administration of 4-6 cycles of therapy according to the Dara-VTD schedule (variable based on the transplant list), patients underwent ASCT followed by consolidation with Dara-VTD (any missing cycles) and maintenance with Lenalidomide 10 mg/day. MRD analysis was performed using next -generation flow cytometry (NGF). FISH was done after plasmacells separation at diagnosis. HR was considered del17p, t4;14, t14,16, amp1q.

Results. 228 patients (M/F ,127/101) were enrolled with a median age of 62 years at diagnosis. Median follow up is 15 months(4-46). Grade 3-4 hematologic toxicities (anemia and/or leukopenia and/or thrombocytopenia) occurred in 7,4% of patients, while non-hematologic toxicities occurred in 21,9% of patients. 14 of 228 patients died (6,14%), including seven (3.07%) due to toxicity/sepsis during induction. Response after four cycles of Dara-VTD, showed 12.9% sCR, 11.29% CR, 52.15% VGPR, 19.35% 4.84% PD. Post -ASCT response was: 36,6% sCR, 17,65% CR, 36,6% VGPR, 5,88% SD, 3,27% PD (>CR 53%). The overall MRD negativity rate was approximately 51.8% pre-ASCT and 77.9% post-ASCT. MRD was tested on a total of 106 pre-ASCT patients, with a sensitivity of 10^-5 in 82 and 10^-6 in 24. Post-ASCT evaluation was performed on 82 patients, with a sensitivity of 10^-5 in 56 and 10^-6 in 26. The overall PFS at 12 months was 92.7%: 94.4% ISS stage I vs. 88.4% stage III (p=0.37); standard cytogenetic risk 96.4% vs. 88% high cytogenetic risk (p=0.05); beta2-microglobulin <3 mg/L 95% vs 87% in patients with a beta2-microglobulin value >5 mg/L (p=0.14); >VGPR post induction 93% vs 83% PR-PD (p=0.01); 96% >VGPR post ASCT vs 78% PR-PD (p=0.0026). Finally, we analyzed PFS stratified by patients who received or did not receive maintenance therapy with lenalidomide after autologous transplantation. A 12-month PFS of 94.9% was observed in patients who received this treatment versus 79.3% at 12 months in patients who did not receive maintenance therapy (p = 0.001).

Conclusions. Real-world data appear to align in terms of feasibility and survivals. MRD negativity and responses seem even deeper in the real-life setting.