(S108) CONSOLIDATION FOLLOWED BY MAINTENANCE VS MAINTENANCE ALONE IN NEWLY DIAGNOSED, TRANSPLANT ELIGIBLE MULTIPLE MYELOMA: A RANDOMIZED PHASE 3 STUDY OF THE EUROPEAN MYELOMA NETWORK (EMN02/HO95 MM TRIAL)

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Abstract: S108

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Background

The role of up-front consolidation therapy for newly diagnosed, transplant-eligible MM (NDMM) patients has not been prospectively addressed in the novel agent era.

Aims

To investigate the efficacy of consolidation therapy in NDMM patients following intensification therapy with VMP or HDM.

Methods

The EMN02/HOVON-95 trial was designed to compare [randomization (R) 1] intensification therapy with 4 cycles of bortezomib-melphalan-prednisone (VMP) vs high-dose melphalan (HDM) and autologous stem cell transplantation (ASCT), either single or double, after induction with bortezomib-cyclophosphamide-dexamethasone (VCD) (M. Cavo et al. ASCO 2016, abstract #8000; ASH 2017, abstract #397). A second randomization to consolidation therapy with bortezomib-lenalidomide-dexamethasone (VRD) vs no consolidation (R2) was performed after intensification, to be followed by lenalidomide maintenance until progression or toxicity in both arms. Primary study end points were progression-free survival (PFS) from R1 and PFS from R2. The second planned interim analysis for R2 was performed in February 2018 when at least 66% (= 343) of the required events for PFS had been observed.

Results

From February 2011 to April 2014, 1510 pts aged ≤ 65 years with symptomatic MM were enrolled, of whom 1499 were eligible. Of these, 1211 were randomized (stratification by ISS stage) to VMP (505 pts) or HDM (1 or 2 ASCT) (706 pts). For R2 892 eligible patients were randomized to no consolidation (arm A; 437 pts) or VRD consolidation (arm B; 455 pts). Median follow up from R2 was 42 months (mo) (IQR 32-49, maximum 71). Investigator assessed response status at time of R2 was ≥ CR (20%), ≥ VGPR (67%), ≥ PR (92%). At the time of analysis, 366 events for PFS after R2 had been reported. 5-year PFS from R2 was 44% in all patients (median 55 mo), 41% in arm A (median 45 mo) and 48% in arm B (median 59 mo). PFS from R2 with adjustment for R1 was prolonged in pts randomized to VRD consolidation (HR=0.77; 95% CI=0.63-0.95; P=0.014), which is consistent with results of the first interim analysis (P. Sonneveld et al. ASH 2016, abstract #242). The PFS benefit from VRD was retained across most predefined subgroups, including revised ISS stage I (Hr=0.77, 95% CI 0.47-1.27) and III (HR=0.76, 95% C 0.40-1.45), low-risk cytogenetics (HR=0.79, 95% CI 0.60-1.05), in patients randomized to either VMP (HR=0.67, 95% CI 0.48-0.94) or HDM (HR=0.84, 95% CI 0.65-1.09), but not in patients with high-risk cytogenetics (del(17p) and/or t(4;14) and/or t(14;16) (HR=1.06, 95% CI 0.70-1.61). At 5 years, OS from R2 was 72% in arm A and 77% in arm B, respectively. Toxicity from VRD was limited with 5% CTCAE grade 4, mainly neutropenia (2%) and thrombocytopenia (2%). The actuarial probability of SPM at 4 years from R2 was 5% vs 6% in both arms.

Conclusion

This second interim analysis confirms the initial promising results of consolidation treatment with VRD followed by lenalidomide maintenance until progression or toxicity as compared to maintenance alone for younger NDMM patients, but further study follow-up is needed. This trial was supported by the Dutch Cancer Society (grant 2010-4798) and by unrestricted grants from Celgene and Janssen.

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