(S202) Isatuximab, lenalidomide, bortezomib and dexamethasone for newly-diagnosed, transplanteligible multiple myeloma: post transplantation interim analysis of the randomized Phase III GMMG-HD7 trial

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Abstract

Background:

Anti-CD38 monoclonal antibodies increase efficacy when added to standard-of-care regimens. In transplant-eligible patients (pts) with newly-diagnosed multiple myeloma (NDMM), we recently demonstrated that the addition of the CD38-mAb isatuximab (Isa) to lenalidomide, bortezomib, and dexamethasone (RVd) induction therapy significantly increased the rates of minimal residual disease (MRD) negativity after three cycles of therapy (Isa-RVd 50% vs. RVd 36%, OR 1.82, 95% CI 1.33-2.48, p<0.001; Goldschmidt H et al., 2022, Lancet Haematology).

However, the depth of response resulting from the combination of Isa-containing induction and high-dose therapy (HDT) followed by autologous stem cell transplantation (ASCT) is still to be determined.

Aims:

In the present interim analysis of the GMMG-HD7 trial we aimed to evaluate MRD and response rates after intensification with HDT and ASCT following induction therapy with Isa-RVd or RVd.

Methods:

Pts with transplant-eligible NDMM at 67 sites in Germany were equally randomized to receive three 42-day cycles of either Isa-RVd or RVd. After induction therapy, pts underwent cyclophosphamide-based stem cell collection and subsequently proceeded to HDT with melphalan (200mg/m2) and ASCT. Second ASCT was recommended if pts achieved less than complete response (CR) after first ASCT or in case of high-risk cytogenetics. Pts were then randomized to receive maintenance with either lenalidomide alone or in combination with Isa for up to 36 months. MRD was assessed by nextgeneration flow cytometry (sensitivity 10-5) and response rates according to the IMWG criteria.

Results:

Between 10/2018 and 09/2020, 662 pts were included in the trial. 660 pts were eligible for intention-to-treat analysis. Baseline characteristics have been described previously and were well balanced. 582 pts completed at least one HDT/ASCT, of which 179 received a second HDT/ASCT (80 after Isa-RVd; 99 after RVd). Based on the ITT population, pts achieved deeper responses in the Isa-RVd vs. the RVd arm (VGPR or better: 82.8% vs. 68.7%; OR=2.19; 95% CI 1.49;3.23, p<0.0001; CR or better: 43.5% vs. 34.0%; OR=1.5, 95% CI 1.08;2.07, p=0.013). Furthermore, significantly more patients achieved MRD negativity (independent of IMWG response) after last ASCT in the Isa-RVd (66.2%) compared to the RVd arm (47.7%) (OR=2.13, 95% CI 1.56;2.92, p<0.001). Detailed subgroup analyses will be presented.

With Isa-RVd, MRD negativity and at least VGPR or CR was seen in 63.4% / 38.1% of pts, respectively, compared to 43.8% / 25.8% in the RVd arm (p<0.001).

Among pts who per protocol remained on study, the MRD negativity rates at end of intensification were 72.0% (219 of 304 pts) after Isa-RVd and 56.5% (157 of 278 pts) following RVd (OR 1.98, 95% CI 1.39; 2.85). MRD assessment at end of intensification was not available for 17 and 10 pts, respectively.

Of 163/109 pts with MRD negativity after induction with Isa-RVd/RVd, the status was confirmed in 140/90 pts after intensification (MRDconfirmed in 85.9/82.6%). Of all pts with available data at both time points, only 6/9 pts lost their MRD negative status, while 66/56 pts converted from MRD positive after induction to MRD negative after intensification. (Figure)

Conclusion:

The present interim analysis of the GMMG-HD7 trial demonstrates that the addition of isatuximab to standard-of-care induction followed by HDT and ASCT results in a significantly higher rate of deep responses and MRD negativity rates in every treatment phase. The trial is ongoing and evaluates the addition of Isa to lenalidomide maintenance treatment following second randomization.

Figure