(QA-54) Efficacy and Safety of Isa-KRd Induction Before Response-Adapted Consolidation in Transplant Eligible Newly Diagnosed Multiple Myeloma: an Interim Analysis of the IFM2020-02 MIDAS Study

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Abstract

Introduction:

In patients (pts) with transplant eligible newly diagnosed multiple myeloma, induction therapy with a quadruplet regimen before autologous stem cell transplant (ASCT) is standard. The phase 3 IFM2020-02 MIDAS (Minimal Residual Disease [MRD] Adapted Strategy) study (NCT04934475) assessed an MRD-driven consolidation and maintenance strategy after isatuximab, carfilzomib, lenalidomide, and dexamethasone (Isa-KRd) induction. Here, we report efficacy and safety data of this induction regimen.

Methods:

Eligible pts (< 66 years old) received 6 cycles of 28 days of Isa-KRd: isatuximab (10 mg/kg; weekly for 4 weeks then biweekly), carfilzomib (20 mg/m2 on day [D]1 cycle [C]1 then 56 mg/m2 D1, 8 and 15), lenalidomide 25 mg/day from D1-D21), dexamethasone (40 mg/week). Cytogenetics risk was assessed at diagnosis (by next generation sequencing [NGS]): Linear predictor (LP) score (using del(17p), t(4;14), del(1p32), gain 1q, trisomy 21 and trisomy 5) defined high risk (HR) if >1. Peripheral stem cells (PSCs) were collected after 3 cycles, G-CSF and plerixafor mobilization. Response was evaluated according to IMWG criteria. MRD was measured by NGS.

Results:

Between December 2021 and July 2023, 791 pts were enrolled in 72 centers. The median age was 59 years [range 25-66]. Sixty-one pts (8%) had SLiM criteria only. MM was classified as ISS III in 120 pts (15%), R-ISS III in 76 (10%). Cytogenetics was evaluated in 757 pts: 8% were HR with a LP score >1 (17% and 32% were HR with the new IMS and the R2-ISS scores, respectively); t(11;14) was present in 26%. Only 5 pts had extramedullary disease at diagnosis, 700 being evaluated by PET-CT; 53 (7%) had circulating plasma cells. All 791 enrolled pts initiated Isa-KRd induction, 766 (97%) had ≥1 PSC mobilization course and 761 had ≥1 apheresis: the median number of CD34+ cells collected was 7.106/Kg. The PSCs collected permitted potential tandem transplant in 719 pts. 757 pts completed 6 cycles of Isa-KRD. The ORR rate was 95%. In the intent-to-treat (ITT) population, 91% of the pts achieved a VGPR or better after induction (95% in the per-protocol [PP] population). 751 pts had post-induction MRD: in the ITT population, the MRD negativity rate was 63% at 10-5 and 47% at 10-6 (66% and 50%, respectively, in the PP population). MRD negativity rates differed significantly with respect to ISS stage, and cytogenetic subgroups: data will be presented at the meeting. During induction, 7 pts had disease progression and 5 died: 1 from disease progression, 2 from cardiac adverts events (AEs), and 2 from other AEs. The most frequently reported grade 3-4 AEs were neutropenia (25%), thrombocytopenia (5%), and infections (7%). Peripheral neuropathy was reported for 6% of pts: mostly grade 1-2.

Conclusion:

Isa-KRd induction resulted in deep responses and high MRD negativity rates; and permitted PSCs to be collected for ASCT(s). No new safety signals were observed. The ongoing MIDAS study needs further follow-up for final analysis.