Abstract: P958

Title: IBERDOMIDE MAINTENANCE AFTER AUTOLOGOUS STEM-CELL TRANSPLANTATION IN PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA: AN UPDATE FROM THE PHASE 2 EMN26 TRIAL

Abstract Type: Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

Iberdomide is a novel oral cereblon E3 ligase modulator with clinically meaningful activity in triple-class refractory multiple myeloma (MM) patients (pts), including those refractory to lenalidomide and pomalidomide. We previously showed that iberdomide maintenance improves response post transplant with a manageable safety profile.

Aims:

Here we present an updated analysis with longer-term follow-up including the first data from cohort 3 with 0.75 mg iberdomide.

Methods:

The EMN26 study (NCT04564703) enrolled MM pts aged ≥18 years, who had achieved at least a partial response (PR) after induction therapy containing a proteasome inhibitor (PI) plus an immunomodulatory drug (IMiD) followed by 1 or 2 autologous stem-cell transplants (ASCT) +/- consolidation, into one of 3 different cohorts (iberdomide 0.75, 1.0, or 1.3 mg on days 1–21 of each 28-day cycle; 40 pts in each cohort). The primary outcome was improvement in response, and secondary outcomes included rate of minimal residual disease (MRD; by next-generation flow) conversion from positive to negative (sensitivity 10-5), safety, and progression-free survival (PFS).

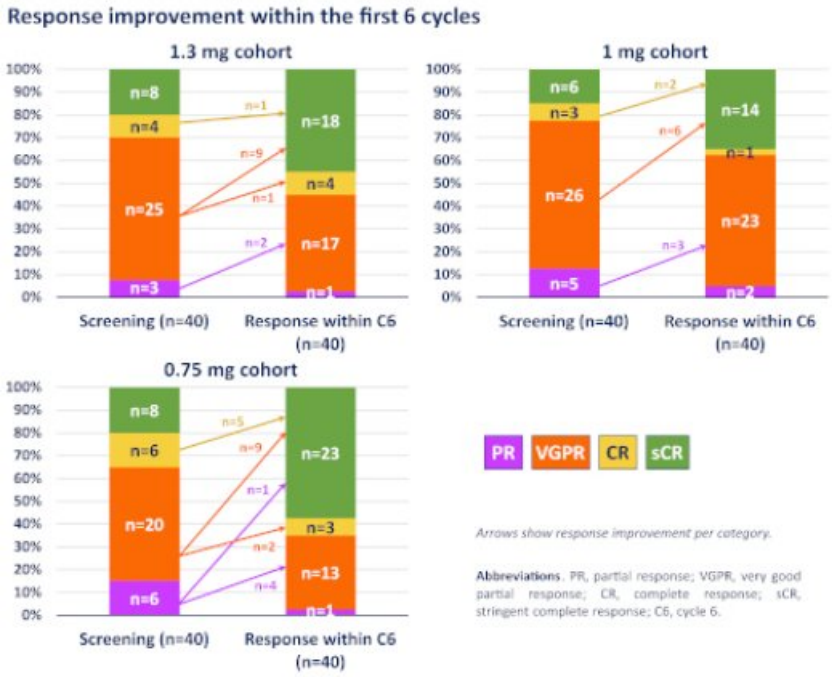
Results:

At data cut-off (Feb. 2, 2024), 40 pts were enrolled in each of the 3 cohorts (total of 120). Median follow-up was 8.4, 21.1, and 18.3 months for the 0.75, 1.0, and 1.3 mg cohorts, respectively (the 0.75 mg was added later). Baseline characteristics were well balanced among the 3 cohorts. Median age of these 120 pts was 59 years, and 54% were male. At diagnosis, 31% of pts presented with Revised International Staging System (ISS) stage 1 disease, 57% with stage 2, and 12% with stage 3. High-risk disease (del(17p), t(4;14), and/or t(14;16)) was present in 21%. All pts received a PI/IMiD-containing induction regimen, which also included daratumumab in 53% of pts. Quadruplet induction was more frequently used in the 0.75 mg cohort (88%), compared to the other 2 cohorts (35% and 38%). Double ASCT was administered to 17% and post-ASCT consolidation to 21%.

After 6 treatment cycles, there was substantial deepening of response in all 3 cohorts, with improvement of response observed in 66% (90% CI 50–79%) of pts in the 0.75 mg, 32% (90% CI 19–48%) in the 1.0 mg, and 41% (90% CI 26–57%) in the 1.3 mg cohorts (*Figure*). These response improvements were significantly higher than the null hypothesis of ≤20% response improvement within 6 months. Response improvement during the first 12 cycles increased to 47% and 59% in the 1.0 and 1.3 mg cohorts, respectively (too early to evaluate for 0.75 mg cohort). MRD conversion from positive to negative occurred in 30%, 32%, and 53% of pts in these 3 cohorts (overall 39%). 12-month PFS was 95%, 87%, and 90% in the 0.75 mg, 1.0 and 1.3 mg cohorts.

The most common grade ≥3 adverse events (AEs) during cycles 1–12 were neutropenia (42% in the 1.0 mg and 52% in the 1.3 mg cohorts) and infections (15% and 10%). In the 0.75 mg cohort during cycles 1–6, grade ≥3 neutropenia occurred in 30% and grade ≥3 infections in 2%. There were no grade ≥3 AEs of thrombocytopenia, anemia, diarrhea, or venous thromboembolism. Only 1 of 120 pts (0.8%) developed grade ≥3 neuropathy.

Conclusion: Iberdomide represents a novel effective maintenance strategy with a favorable safety profile and superior response improvement than what has been observed with lenalidomide maintenance (26% at 6 and 31% at 12 months in the EMN02 study). These data support the investigation of iberdomide vs. lenalidomide maintenance in the ongoing phase 3 registrational EXCALIBER maintenance trial.



Keywords: Clinical trial, Multiple myeloma, Maintenance, Post-transplant