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ORAL ABSTRACTS

653.MULTIPLE MYELOMA: PROSPECTIVE THERAPEUTIC TRIALS

Iberdomide Maintenance after Autologous Stem-Cell Transplantation in Newly Diagnosed MM: First Results of the Phase 2 EMN26 Study

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Background. Iberdomide is a novel oral cereblon E3 ligase modulator (CELMoD ™) with enhanced direct antitumor effects and immune stimulatory effects, compared to lenalidomide or pomalidomide. In the ongoing phase 1/2 CC-220-MM-001 study, iberdomide plus dexamethasone had a favorable safety profile and demonstrated clinically meaningful activity in triple-class refractory multiple myeloma (MM) patients, including those refractory to lenalidomide and pomalidomide (IMiDs ®). Based on these data, we aimed to evaluate the safety and clinical activity of 3 different doses of iberdomide as a novel maintenance treatment post-transplant in newly diagnosed MM patients. Here we report results from the first interim analysis for patients who have been treated with at least 6 treatment cycles, or discontinued treatment earlier.

Methods. The EMN26 study is a multicohort, phase 2 study conducted in 4 European countries. Patients aged 18 years or older with MM, who had achieved at least a partial response (PR) after induction therapy containing a proteasome inhibitor (PI) plus IMiD followed by single or double autologous stem-cell transplantation (ASCT) +/- consolidation, were enrolled

into one of 3 different cohorts (iberdomide 0.75, 1.0, or 1.3 mg on days 1-21 of each 28-day cycle; treatment continued until progression or unacceptable toxicity; 40 patients in each cohort). The primary outcome is improvement in response, and secondary outcomes include safety and progression-free survival (PFS). Response was evaluated at screening and after every cycle (bone marrow analysis was done at screening, at 6 and 12 months after treatment initiation, and to confirm (s)CR). This trial is ongoing and is registered with ClinicalTrials.gov (NCT04564703).

Results. At data cut-off (May 31, 2023) 31 patients were enrolled in the 0.75 mg cohort, and 40 patients each in the 1.0 and 1.3 mg cohorts (total of 111). A total of 69 patients had received ≥6 cycles of iberdomide treatment or discontinued earlier (n=34 in 1.0 mg cohort; n=35 in 1.3 mg cohort; n=0 in 0.75 mg cohort [this cohort was added later]). Median age of these 69 patients was 59 years, and 57% were male. At diagnosis, 37% of patients presented with International Staging System (ISS) stage 1 disease, 35% with ISS stage 2, and 28% with stage 3. High-risk disease (del(17p), t(4;14), and/or t(14;16)) was present in 14% of patients. All patients received a PI/IMiD-containing induction regimen which also included daratumumab in 41% of patients. Double ASCT was administered to 19% and post-ASCT consolidation to 7%. Best response at the time of enrollment in the study was PR in 15%, very good (VG)PR in 59%, complete response (CR) in 12%, stringent (s)CR in 15% [≥CR: 26%] in the 1.0 mg cohort, and PR in 3%, VGPR in 69%, CR in 11%, sCR in 17% [≥CR: 29%] in the 1.3 mg cohort. After 6 treatment cycles, there was comparable deepening of response in both cohorts (1.0 mg cohort: PR 6%, VGPR 44%, CR 3%, sCR 47% [≥CR: 50%]; 1.3 mg cohort: PR 3%, VGPR 37%, CR 9%, sCR 51% [≥CR: 60%]). Improvement of response was reported in 48% (90% CI 32-65%) of patients treated with 1.0 mg iberdomide and 45% (90% CI 29-62%) in the 1.3 mg iberdomide cohort (*Figure*), which are significantly higher than the null hypothesis of ≤20% response improvement within 6 months. The most common grade 3 or worse adverse events (AEs) during cycles 1-6 were neutropenia (21% in 1.0 mg cohort and 46% in 1.3 mg cohort), infections (3% and 14%), fatigue/asthenia (12% and 14%). There were no events of ≥grade 3 thrombocytopenia, anemia, diarrhea, VTE, or neuropathy. Dose reductions were used to manage AEs in 18% of patients in the 1.0 mg cohort and 31% in the 1.3 mg cohort. Treatment discontinuation occurred in 3 patients in 1.0 mg cohort (1 due to AE, 2 PD), and 4 patients in 1.3 mg cohort (2 due to AE, 1 PD, and 1 death [unknown cause]). PFS at 6 months was 97% and 94% in the 1.0 and 1.3 mg cohorts. With longer follow-up, results from the 0.75 mg cohort and MRD conversion data will be presented at the meeting.

Conclusions. Iberdomide represents a novel effective post-ASCT maintenance strategy with a favorable safety profile and superior response improvement at 6 months than what has been observed with lenalidomide maintenance (26% at 6 months in the EMN02 study). Additional follow-up is needed to define the recommended maintenance dose that will be used in the randomized phase 3 EXCALIBER maintenance study, which will evaluate iberdomide vs. lenalidomide maintenance post-ASCT.

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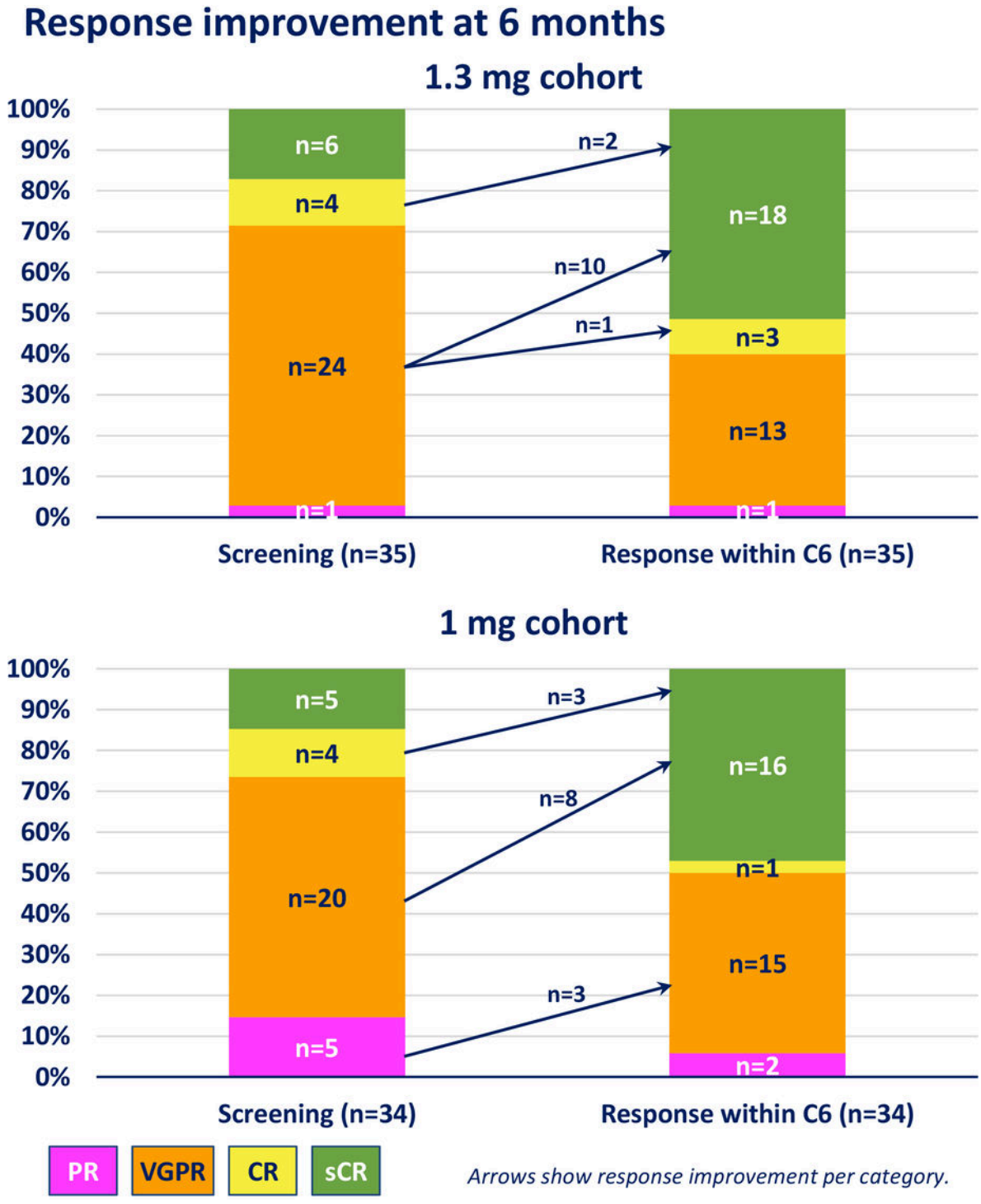
OffLabel Disclosure: This presentation includes information or discussion of the off-label use of a drug or drugs for the treatment of multiple myeloma: iberdomide.



Abbreviations. PR, partial response; VGPR, very good partial response; CR, complete response; sCR, stringent complete response; C6, cycle 6.

Figure 1

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