

MagnetisMM-30: A phase 1b, open-label study of elranatamab in combination with iberdomide in patients with relapsed or refractory multiple myeloma (RRMM).

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Background: Elranatamab (ELRA), a BCMA–CD3 bispecific antibody, induced deep and durable responses with a manageable safety profile as a single agent in patients (pts) with RRMM enrolled in the phase 2 registrational MagnetisMM-3 study (Lesokhin et al, *Nat Med* 2023). Iberdomide (IBER) is a novel CELMoD agent that enhances antitumor activity and immunomodulatory activity in pts with RRMM (Lonial et al, *Lancet Haematol* 2022). While IBER in combination with ELRA has not been evaluated clinically, it may provide additional benefit to pts with RRMM based on the mechanisms of action of this novel combination. **Methods:** MagnetisMM-30 (NCT06215118) is a phase 1b, open-label, prospective study evaluating the safety, efficacy, and pharmacokinetics of ELRA in combination with IBER in pts with RRMM. The study has 2 parts: Part 1 guided by BOIN for dose-escalation and Part 2, randomized for dose optimization. In Part 1, after 2 step-up priming doses of subcutaneous (SC) ELRA followed by 1 full dose, pts will receive SC ELRA at dose level (DL) 1 or DL2 in 28-day cycles. IBER will be given daily for 21 days of each cycle. In DL1, pts will receive ELRA weekly followed by every 2 weeks (Q2W) and finally Q4W. In DL2, pts will receive ELRA Q2W followed by Q4W, with a higher IBER dose. If DL1 or DL2 is not tolerated, IBER dosing will be lowered (DL-1 and DL-2). Once 2 combination dose levels are selected from Part 1 as the recommended doses for expansion for ELRA and IBER, pts in Part 2 will be randomized 1:1 (stratified by the number of prior lines of therapy [LOTs; 1 vs >1]) to dose levels A or B. Key inclusion criteria are pts aged ≥ 18 years with a MM diagnosis per IMWG criteria, Eastern Cooperative Oncology Group performance status of 0–1, adequate organ and bone marrow function, and disease relapsed or refractory to the last antitumor regimen per IMWG response criteria. Pts who received 2–4 or 1–3 prior LOTs, including ≥ 1 immunomodulatory drug (IMiD) and ≥ 1 proteasome inhibitor (PI), are eligible for Parts 1 and 2, respectively. All pts must have received ≥ 2 consecutive cycles of an IMiD-containing regimen and ≥ 2 consecutive cycles of a PI or PI-containing regimen. Key exclusion criteria are pts with stem cell transplant ≤ 12 weeks prior to enrollment; active, uncontrolled infection; prior treatment with BCMA-directed or CD3 redirecting therapy or prior CELMoD agents (ie, IBER or mezigdomide). Primary endpoints are dose-limiting toxicities during the first cycle of treatment (Part 1) and AEs and lab abnormalities (Part 2). Secondary endpoints include AEs and lab abnormalities (Part 1 only), ORR, CRR, time-to-event outcomes, pharmacokinetics, minimal residual disease negativity rate, and immunogenicity. This study is ongoing; Part 1 and Part 2 will enroll up to approximately 36 and 60 pts, respectively. Clinical trial information: NCT06215118. Research Sponsor: Pfizer.