LEMZOPARLIMAB (TJ011133), AN ANTI-CD47 ANTIBODY, WITH/WITHOUT DEXAMETHASONE PLUS ANTI-MYELOMA REGIMENS FOR RELAPSED/REFRACTORY MULTIPLE MYELOMA: A PHASE 1B DOSE ESCALATION AND EXPANSION STUDY

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Background Despite therapeutic advancements for multiple myeloma (MM), most patients with MM develop relapsed/refractory (R/R) disease, which is associated with high mortality and highlights an unmet need for novel treatments. A key characteristic of MM cells is the overexpression of CD47, which downregulates phagocytosis, thereby allowing malignant plasma cells to evade destruction by the immune system. Blocking CD47 with lempzoparlimab, an anti-CD47 monoclonal antibody, may enhance macrophage-mediated anti-tumor activity. This study will characterize the safety, dose-limiting toxicity, and recommended dosing of lempzoparlimab (TJ011133) with or without dexamethasone and combined with other anti-myeloma regimens in patients with R/R MM.

Methods This phase 1b, open-label, dose-escalation and expansion study (NCT04895410) will enroll adults with R/R MM, an Eastern Cooperative Oncology Group Performance Status ≤2, prior treatment history (varies based on treatment arm; Figure 1), and measurable disease (serum monoclonal paraprotein [M-protein] ≥0.5 g/dL, urine M-protein ≥200 mg/24 hours, or serum-free light chain ≥100 mg/L). Patients will be enrolled in 2 phases (escalation and expansion), divided into 4 arms to receive treatment in 28-day cycles (figure 1): (A) lempzoparlimab ± dexamethasone; (B) lempzoparlimab + dexamethasone + pomalidomide (4 mg orally daily [Days 1–21]); (C) lempzoparlimab + dexamethasone + carfilzomib (56 mg/m² intravenously, 6 doses/cycle [first 2 doses in Cycle 1: 20 mg/m²]); and (D) lempzoparlimab + dexamethasone + daratumumab (1800 mg subcutaneously [Cycle 1, start on Day 2; Cycles 1–2, once weekly; Cycles 3–6, every 2 weeks; Cycles ≥7, Day 1]). Dexamethasone will be administered orally twice weekly at 20 mg for Arm C, and orally or intravenously weekly at 40 mg for other arms. Dose escalation will follow Bayesian optimal interval design. Once maximum tolerated dose/recommended phase 2 dose (RP2D) is determined, patients will be enrolled in the expansion. Treatment discontinuation criteria are: unacceptable toxicity, disease progression, consent withdrawal, or investigator's discretion. The primary endpoint is determination of the RP2D. Secondary endpoints include safety and efficacy measures. Time-to-event endpoints will be analyzed using the Kaplan–Meier method.

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Trial Registration ClinicalTrials.gov: NCT04895410

Ethics Approval The protocol, informed consent form(s), recruitment materials, and all patient materials will be submitted to the Independent Ethics Committee/Institutional Review Board for review and approval.

Abstract 448 Figure 1 Study schematic

The dose escalation phase will follow BOIN; it will start with lempzoparlimab (TJ011133) monotherapy at DL1 in Arm A. If DL1 is not tolerated as monotherapy or as combination therapy, DL -1 will be evaluated. Investigation of combination arms will start after evaluation of monotherapy.

Arms A, B, C and D will include patients with R/R MM after progressing on defined therapies and number of prior lines of therapy.

BOIN, Bayesian optimal interval; DL, dose level; MM, multiple myeloma; R/R, relapsed/refractory.

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