S193 TECLISTAMAB, A B-CELL MATURATION ANTIGEN (BCMA) × CD3 BISPECIFIC ANTIBODY, IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA: UPDATED PHASE 1 RESULTS

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

Keywords: Immunoglobulin Immunotherapy Multiple myeloma

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Background: B-cell maturation antigen (BCMA)-targeted immunotherapies are promising treatment options for patients with relapsed/refractory multiple myeloma (MM). Teclistamab (JNJ-64007957) is a bispecific immunoglobulin G4 antibody that binds to both BCMA and CD3 to redirect CD3+ T cells to BCMA-expressing MM cells.

Aims: To report updated results from the first-in-human phase 1 study of teclistamab in patients with relapsed/refractory MM who were treated at the recommended phase 2 dose (RP2D).

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Methods: Eligible patients had relapsed/refractory MM or were intolerant to established therapies. The primary objectives of the study were to identify the RP2D (part 1) and to characterize the safety and tolerability of teclistamab at the RP2D (part 2). Teclistamab was given either intravenously (IV; range 0.3–19.2 μg/kg biweekly; range 19.2–720 μg/kg weekly) or subcutaneously (SC; range 80.0–3000 μg/kg weekly) in different cohorts, with step-up dosing for doses ≥38.4 μg/kg. Adverse events (AEs) were graded by Common Terminology Criteria for Adverse Events v4.03, and cytokine release syndrome (CRS) was graded by Lee et al 2014 criteria. Response was assessed per International Myeloma Working Group criteria. All patients provided informed consent.

Results: As of Feb 4, 2021, 156 patients had received teclistamab IV (n=84) or SC (n=72). The identified RP2D of weekly SC 1500 μg/kg teclistamab with 60.0 and 300 μg/kg step-up doses, was given to 40 patients; the median follow-up was 4.3 months (range 1.1–10.4+). Of the patients treated at the RP2D, the median age was 62.5 years (range, 39–84), 65% were men and a median of 5 prior lines of therapy was received (range 2–11; 100% triple-class exposed; 65% penta-drug exposed; 83% triple-class refractory; 35% penta-drug refractory; 85% refractory to their last line of therapy). No dose-limiting toxicities occurred at the RP2D in part 1 of the study. The most common AEs at the RP2D were CRS (70%; no grade 3/4 events) and neutropenia (60%; 40% were grade 3/4); grade 1 neurotoxicity was reported in 1 (3%) patient. The median time to CRS onset occurred later with SC dosing compared with IV dosing (day after SC injection vs. day of IV infusion). The overall response rate in response-evaluable patients treated at the RP2D (n = 40) was 65%; 58% of patients achieved a very good partial response or better, and 30% of patients achieved a complete response (CR) or better. The median time to first confirmed response was 1.0 month (range 0.2–3.1). At the RP2D, the median duration of response was not reached with 23/26 responders (88%) alive and continuing treatment at a median follow-up of 5.3 months (range 1.2–10.4+). Responses continued to deepen over time. Of 14 evaluable patients across all cohorts, 9 with CR were minimal residual disease–negative at 10-6. At the RP2D, teclistamab exposure was sustained across the dosing interval and exceeded target levels. Consistent T cell activation was also observed at the RP2D.

Conclusion: At the RP2D of weekly 1500 μg/kg SC, teclistamab was well-tolerated and demonstrated encouraging efficacy with durable, deepening responses, warranting further investigation as monotherapy and in combination with other agents. With the extended exposure profile at the RP2D and delayed and low-grade CRS observed with SC administration, alternative SC dosing strategies are being explored.