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TALQUETAMAB, A G PROTEIN-COUPLED RECEPTOR FAMILY C GROUP 5 MEMBER D (GPRC5D) × CD3 BISPECIFIC ANTIBODY, IN RELAPSED/REFRACTORY MULTIPLE MYELOMA: UPDATED RESULTS OF A PHASE 1, FIRST-IN-HUMAN STUDY

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Background:

As patients with multiple myeloma (MM) continue to relapse on current therapies, new immunotherapy targets are needed. G protein-coupled receptor family C group 5 member D (GPRC5D) is an orphan receptor that is expressed on malignant plasma cells in MM. Talquetamab (JNJ-64407564) is a bispecific immunoglobulin G4 antibody that binds to CD3 and the novel target GPRC5D to redirect T cells to kill MM cells.

Aims:

To report updated phase 1 results of patients with relapsed/refractory MM treated with talquetamab at the recommended phase 2 dose (RP2D).

Methods:

Eligible pts with MM who had relapsed or refractory disease or were intolerant to standard therapies, were administered talquetamab either intravenously (IV; range 0.5–180 µg/kg) or subcutaneously (SC; range 5.0–800 µg/kg) in a weekly or biweekly dosing schedule. The primary objectives of the study were to identify the RP2D (part 1) and to characterize the safety and tolerability of talquetamab at the RP2D (part 2). Adverse events (AEs) were graded by Common Terminology Criteria for Adverse Events (CTCAE) v4.03, and cytokine release syndrome (CRS) was graded per Lee 2014 criteria. Response was assessed per International Myeloma Working Group criteria. All patients provided informed consent.

Results:

As of Feb 8, 2021, 174 patients received talquetamab IV (n=102) or SC (n=72). Across parts 1 and 2 of the study, 28 patients were treated at the RP2D, identified as weekly SC 405 µg/kg, with 10.0 and 60.0 µg/kg step-up doses. Patients treated at the RP2D had a median age of 61.5 years (range 46–80 years) and had received a median of 5.5 prior lines of therapy (range 2–14; 100%/79% triple-class/penta-drug exposed; 71%/18% triple-class/penta-drug refractory; 86% refractory to last line of therapy; 21% with prior B-cell maturation antigen–directed therapy). No dose-limiting toxicities occurred at the RP2D in part 1 of the study. The most common AEs at the RP2D were CRS

(79%; 4% were grade 3; median time to onset was day after SC dose), neutropenia (64%; 54% were grade 3/4), anemia (57%; 29% were grade 3/4) and dysgeusia (57%; all were grade 1/2). Infections were reported in 32% of patients (4% were grade 3/4) and neurotoxicity reported in 7% (no grade 3/4 events). In all, 75% of patients who received the RP2D had skin-related AEs, none of which were grade 3/4, including 18% with nail disorders. In response-evaluable patients (n=24), the overall response rate at the RP2D was 63%, with 50% reaching very good partial response or better; 9/17 (53%) evaluable triple-class refractory patients and 3/3 (100%) penta-drug refractory patients had a response. The median time to first confirmed response at the RP2D was 1.0 month (range 0.2–3.8). Responses were durable and deepened over time; the median follow-up was 6.2 month [range 2.7–9.7+] for responders at the RP2D. Talquetamab exposure at the RP2D was maintained over the maximum EC target level from an ex vivo cytotoxicity assay. Consistent T cell activation was also observed at the RP2D.

Summary/Conclusion:

Talquetamab, at the RP2D of weekly 405 μg/kg SC, demonstrated a high clinical response rate and was well-tolerated in patients with relapsed/refractory MM. Based on the pharmacokinetic data, other SC dosing strategies are also being explored. The promising efficacy and safety profile, and the convenience of SC dosing support monotherapy development and combination approaches with this novel agent.

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