

S182 TALQUETAMAB, A G PROTEIN-COUPLED RECEPTOR FAMILY C GROUP 5 MEMBER D X CD3 BISPECIFIC ANTIBODY, IN RELAPSED/REFRACTORY MULTIPLE MYELOMA: UPDATED EFFICACY AND SAFETY RESULTS FROM MONUMENTAL-1

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Background: G protein-coupled receptor family C group 5 member D (GPCR5D) is a promising therapeutic target for multiple myeloma (MM) immunotherapy. GPCR5D has limited expression in healthy human tissue but is highly expressed on malignant plasma cells. Talquetamab (JNJ-64407564) is a first-in-class, GPCR5D x CD3 bispecific IgG4 antibody that induces T cell-activated lysis of GPCR5D+ MM. MonumenTAL-1 is a phase 1 trial evaluating the safety and preliminary efficacy of talquetamab in patients with relapsed/refractory MM (RRMM) (NCT03399799).

Aims: We report updated results from MonumenTAL-1 with additional patients and longer follow-up.

Methods: Patients with RRMM or who were intolerant to standard therapies were eligible; prior treatment with B-cell maturation antigen-directed therapies was allowed. The primary objectives were to identify the recommended phase 2 doses (RP2Ds) (part 1) and assess the safety and tolerability of talquetamab at the RP2Ds (part 2). Based on the collective safety, preliminary efficacy, pharmacokinetics (PK), and pharmacodynamics (PD) data, 2 RP2Ds of talquetamab were identified: 405 µg/kg SC QW (n=30) and 800 µg/kg SC Q2W (n=44). To mitigate severe cytokine release syndrome (CRS), step-up dosing was used. Administration of required premedications were limited to step-up doses and the first full dose of talquetamab. Adverse events (AEs) were graded by CTCAE v4.03, and CRS events were graded per Lee et al 2014 criteria. Responses were assessed by the investigators as per International Myeloma Working Group criteria.

Results: As of Jan 17, 2022, patients in the 405 µg/kg /800 µg/kg groups, respectively, received a median of 6/5 prior lines of therapy, 100%/98% were triple-class (TC) exposed, and 77%/75% were TC refractory, and median follow-up (range) was 11.7 (1.0–21.2)/4.2 (0.7–13.7) months. AEs were mostly grade 1 or 2, and cytopenias and CRS were the most commonly reported AEs. Cytopenias, including neutropenia (67%/36%; grade 3/4: 53%/23%), were mostly limited to step-up and cycle 1–2 doses, reversible, and generally resolved within 1 week. CRS (77%/80%; grade 3: 3%/0%) were mostly reported during step-up dosing. Infections were reported in 47%/34% (grade 3/4: 7%/9%) of patients. 83%/75% of patients reported skin-related and nail disorder AEs (most commonly skin exfoliation: 37%/39% [all grade 1 and 2]). Dysgeusia (63%/57%) was generally mild and managed with dose adjustments. Response-evaluable patients had overall response rates of 70% (21/30 patients)/64% (28/44 patients). Very good partial response or better rates were 57%/52%, and median time to first confirmed response (range) was 0.9 (0.2–3.8)/1.2 (0.3–6.8) months. Median duration of response will be reported. No deaths from drug-related AEs were reported. Both RP2Ds showed comparable PK and PD profiles.

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Summary/Conclusion: Both RP2Ds of talquetamab appear tolerable with comparable safety and PK profiles. Talquetamab demonstrated highly promising efficacy as a novel, first-in-class therapy for heavily pretreated patients with RRMM.

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