S188 TECLISTAMAB IN COMBINATION WITH DARATUMUMAB, A NOVEL, IMMUNOTHERAPY-BASED APPROACH FOR THE TREATMENT OF RELAPSED/REFRACTORY MULTIPLE MYELOMA: UPDATED PHASE 1B RESULTS

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Background:
Teclistamab (JNJ-64007957) is a B-cell maturation antigen (BCMA) × CD3 T-cell redirecting bispecific antibody currently under investigation in patients with relapsed/refractory multiple myeloma (RRMM). Daratumumab is a CD38-targeting monoclonal antibody with direct on-tumor and immunomodulatory mechanisms of action. The preliminary results from the phase 1b multicohort TRIMM-2 study showed tolerable safety with no overlapping toxicities, and encouraging efficacy, supporting the combination of teclistamab with daratumumab for the treatment of RRMM.

Aims:
We report updated results from the TRIMM-2 study with additional patients and longer follow-up.

Methods:
Eligible patients were ≥18 years of age with a MM diagnosis and previously treated with ≥3 prior lines of therapy (including a proteosome inhibitor [PI] and immunomodulatory drug [IMiD]) or were double-refractory to a PI and IMiD. Patients who had received anti-CD38 therapy ≤90 days prior were excluded. Written informed consent was obtained from all eligible patients. Patients received subcutaneous (SC) daratumumab 1800 mg per approved schedule and teclistamab SC 1.5–3 mg/kg once weekly or every 2 weeks. Primary objectives of the study were to identify the recommended phase 2 dose for the teclistamab and daratumumab combination and to assess safety of the combination. Responses were assessed by IMWG criteria. Adverse events (AEs) were graded per CTCAE v5.0, except for cytokine

release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS), which were graded per ASTCT guidelines.

Results:

At the Jan 13, 2022 data cutoff, the median follow-up was 7.2 months (range 0.1–16.6). Among the safety population (N=46), 52% were females, and the median age was 67 years (range 50–79). Patients received a median of 6 prior lines of therapy (range 2–17); 74% of patients were triple-class exposed; 63% were penta-drug exposed, and 15% were anti-BCMA exposed. Overall, 91% of patients had ≥1 AE of any grade; 78% had grade 3/4 AEs. The most common AE was CRS (61%; all grade 1/2); median time to onset was 2 days and median duration was 2 days. Other AEs included neutropenia (54%; grade 3/4 50%), anemia (46%; grade 3/4 28%), thrombocytopenia (33%; grade 3/4 28%), and diarrhea (33%; grade 3/4 2%). Infections occurred in 29 patients (63%; grade 3/4 28%). One patient had grade 1 ICANS that was fully resolved. Among 37 response-evaluable patients, the overall response rate was 78% (29/37); 27 patients (73%) had very good partial response (VGPR) or better (Table). While the median duration of response was not reached, median time to first response across dosing cohorts was 1.0 month (range 0.9–2.8). Upregulation of CD38+/CD8+ T cells and proinflammatory cytokines was observed after teclistamab dosing in combination with daratumumab, supporting potential synergy of the combination in patients with prior anti-CD38 exposure. Updated results will be presented.

Table. Responses in evaluable patients[a] in teclistamab + daratumumab cohorts

	Dara 1800 mg + Tec 1.5 mg/kg QW (n=20)[b]	Dara 1800 mg + Tec 3 mg/kg QW (n=4)	Dara 1800 mg + Tec 3 mg/kg Q2W (n=13)
Overall response, n	15	4	10
VGPR or better, n	14	4	9
Complete response or better, n	6	2	1

dara, daratumumab; QW, once weekly; Q2W, every 2 weeks; tec, teclistamab; VGPR, very good partial response.
[a]Patients who received ≥1 study treatment and had ≥1 postbaseline response evaluation.
[b]8 patients switched to tec 3 mg/kg Q2W (3 at cycle [C] 4, 3 at C5, 1 at C7, and 1 at C9).

Conclusion:

Teclistamab in combination with daratumumab is a novel immunotherapy approach that may yield improved clinical efficacy in heavily pretreated patients with RRMM.

Keyword(s):

B-cell maturation antigen, Bispecific, Immunotherapy, Multiple myeloma