Updated Results from MajesTEC-1: Phase 1/2 Study of Teclistamab, a B-Cell Maturation Antigen x CD3 Bispecific Antibody, in Relapsed/Refractory Multiple Myeloma

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Introduction:

Teclistamab (JNJ-64007957) is a T-cell redirecting, bispecific IgG4 antibody that targets both B-cell maturation antigen (BCMA) and CD3 receptors to induce T-cell mediated cytotoxicity of BCMA-expressing myeloma cells. Teclistamab is under investigation in MajesTEC-1, an ongoing phase 1/2 study in patients (pts) with heavily pretreated relapsed/refractory multiple myeloma (RRMM). Results from the phase 1 study (parts 1 and 2; NCT03145181) indicated that teclistamab is well tolerated at the recommended phase 2 dose (RP2D) and has encouraging efficacy, with an overall response rate (ORR) of 65% and very good partial response or better (≥VGPR) rate of 58% in 40 pts after a median of 6.1 mo of follow-up. Here we report for the first time initial data from the phase 2 portion of MajesTEC-1 (part 3; NCT04557098) and updated results for phase 1 pts treated at the RP2D.

Methods:

Pts (aged ≥18 years) were diagnosed with MM per International Myeloma Working Group (IMWG) criteria, had measurable disease and were exposed to a proteasome inhibitor, immunomodulatory drug, and anti-CD38 antibody. In phase 1, pts were relapsed, refractory or intolerant to established therapies. In phase 2, pts received ≥3 prior lines of therapy. The primary objectives in phase 1 were to identify the RP2D and to characterize safety and tolerability of teclistamab at the RP2D. The primary objective in phase 2 is to evaluate the efficacy of teclistamab at the RP2D (primary endpoint: ORR). Pts treated at the RP2D received a weekly dose of subcutaneous teclistamab 1500 µg/kg following step-up doses of 60 and 300 µg/kg. Responses reported here were investigator-assessed per IMWG criteria. Adverse events (AEs) are graded according to CTCAE v4.03. Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) were graded according to ASTCT criteria.

Results:

As of June 14, 2021, 159 pts (median age 64.0 y [range 33-84]; 15% ≥75 y; 59% male) were treated at the RP2D (phase 1: 40 pts; phase 2: 119 pts). Pts received a median of 5 prior lines of therapy (range: 2-15); 100% were triple-class exposed, 69% were penta-drug exposed, 77% were triple-class refractory, and 29% were penta-drug refractory.

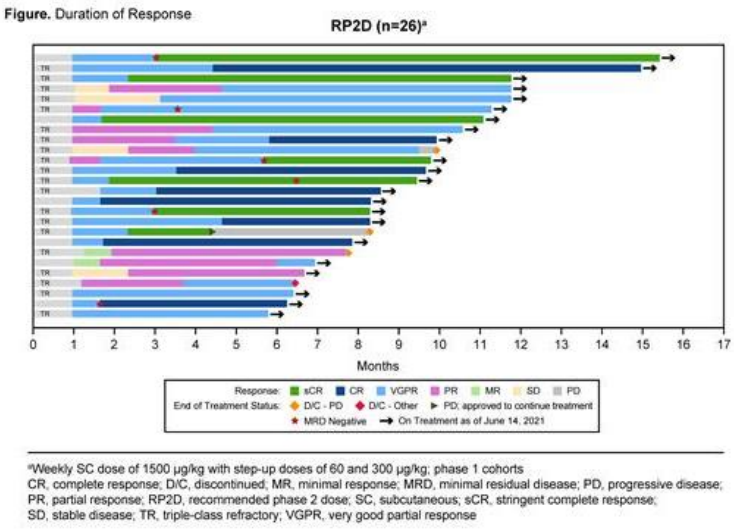
As of the clinical cutoff, no new safety signals were identified in phase 2. The most common nonhematologic AEs in all 159 pts treated at the RP2D were CRS (67%; grade 1/2: 99%; 1 pt had a transient grade 3 event; median time to onset 2 days [range 1-6]; median duration 2 days [range 1-9]), injection site erythema (23%; all grade 1/2), and fatigue (22%; grade 3/4: 2%). The most common hematologic AEs were neutropenia (53%; grade 3/4: 45%), anemia (41%; grade 3/4: 27%), and thrombocytopenia (33%; grade 3/4: 18%). Four pts (2.5%) developed ICANS (all grade 1/2; all resolved). Pharmacokinetic and pharmacodynamic data from phase 2 support earlier phase 1 findings. Teclistamab exposure at the RP2D was sustained across the dosing interval and exceeded target exposure levels. Pharmacodynamic data for phase 1/2 pts treated at the RP2D showed induction of proinflammatory cytokines and T-cell activation, consistent with teclistamab's mechanism of action.

At clinical cutoff for this abstract, efficacy data for the phase 2 study are immature. At a median follow-up of 8.2 mo (range 1.2-15.2), response rates in the 40 phase 1 pts treated at RP2D were consistent with previously presented data (ORR: 65% [95% CI 48-79]; ≥VGPR rate: 60% [95% CI 43-75]; complete response or better rate: 40% [95% CI 25-57]). Responses deepened over time, and with longer follow-up of responders compared with previously presented data (median follow-up of 9.5 mo vs 7.1 mo) remained durable (Figure). No additional responders had disease progression, and 85% (22/26) of responders are continuing on treatment, including 1 pt with 15.2 mo of follow-up. Median duration of response (DOR) has not been reached; the 6-month DOR rate is 90% [95% CI 63-97]. The efficacy data will be updated at the time of congress to include a minimum follow-up of ~6 mo for 150 pts treated at the RP2D (prior to March 19, 2021).

Conclusions:

Evaluation of teclistamab at the RP2D in 159 pts provides robust data to support safety; inclusion of phase 2 pts at the time of presentation will provide more robust efficacy data. Data from MajesTEC-1 continue to show that teclistamab monotherapy induces deep and durable responses in heavily pretreated pts with RRMM with a manageable safety profile.

Figure 1:



[a]Weekly SC dose of 1500 µg/kg with step-up doses of 60 and 300 µg/kg; phase 1 cohorts
CR, complete response; D/C, discontinued; MR, minimal response; MRD, minimal residual disease; PD, progressive disease; PR, partial response; RP2D, recommended phase 2 dose; SC, subcutaneous; sCR, stringent complete response; SD, stable disease; TR, triple-class refractory; VGPR, very good partial response