180 Updated Phase 1 Results of Teclistamab, a B-Cell Maturation Antigen (BCMA) x CD3 Bispecific Antibody, in Relapsed and/or Refractory Multiple Myeloma (RRMM)

Author(s): ***Alfred L. Garfall, MD***[1], *Saad Z. Usmani, MD, MBBS, MBA*[2], *María-Victoria Mateos*[3], *Hareth Nahi, MD, PhD*[4*], *Niels W.C.J. Van De Donk*[5], *Jesus F. San-Miguel, MD, PhD*[6], *Albert Oriol Rocafiguera, MD*[7*], *Laura Rosinol, MD, PhD*[8*], *Ajai Chari, MD*[9], *Manisha Bhutani, MD*[10], *Lixia Pei, PhD*[11*], *Raluca Verona, PhD*[12*], *Suzette Girgis, PhD, BPharm, MS*[11], *Tara Stephenson, PhD*[11*], *Jenna D. Goldberg, MD*[11*], *Arnob Banerjee, MD*[11*] *and Amrita Krishnan, MD*[13]

[1]*Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA*

[2]*Levine Cancer Institute, Charlotte, NC*

[3]*Hospital Clinico Universitario de Salamanca, Salamanca, Spain*

[4]*Karolinska University Hospital at Huddinge, Stockholm, Sweden*

[5]*Department of Hematology, Cancer Center Amsterdam, Amsterdam UMC, VU University Medical Center, Amsterdam, Netherlands*

[6]*Clinica Universidad de Navarra, Pamplona, Spain*

[7]*Institut Català d'Oncologia and Institut Josep Carreras. Hospital Germans Trias i Pujol, Badalona, Barcelona, Spain*

[8]*Hospital Clínic, Barcelona, Spain*

[9]*Mt. Sinai School of Medicine, New York, NY*

[10]*Levine Cancer Institute, Atrium Health, Charlotte, NC*

[11]*Janssen R&D, Spring House, PA*

[12]*Janssen Research & Development, Spring House, PA*

[13]*City of Hope, Duarte, CA*

Background

MM inevitably relapses and becomes refractory to treatment, representing a patient (pt) population with unmet needs. Teclistamab (JNJ-64007957) is a bispecific BCMA x CD3 antibody that induces T cell-mediated cytotoxicity against BCMA-expressing MM cells. Previously presented results from an ongoing study of teclistamab in RRMM (NCT03145181) included a 67% objective response rate [ORR] for the 270 µg/kg dose administered intravenously (iv) (Usmani et al, ASCO 2020 Oral Presentation #100). Here we present updated results and newly available data for subcutaneous (sc) administration.

Methods

Pts have MM that is RR to established therapies. The primary objective is to identify a recommended phase 2 dose(s) (RP2D). Multiple sc and iv doses ± step-up doses were explored. Adverse events (AEs) were graded per CTCAE v4.03 and cytokine release syndrome (CRS) per Lee *et al* 2014. Response was investigator-assessed using IMWG criteria; minimal residual disease (MRD) in bone marrow was assessed by next generation sequencing.

Results

As of 20 Jul 2020, iv teclistamab (0.3–720 µg/kg) and sc teclistamab (80–3000 µg/kg) were received by 84 and 44 pts, respectively. Overall, median age was 64 y (24–82), median number of prior lines of therapies (LOT) was 6 (2–14), 95%/79% triple-class exposed/refractory, 70%/38% penta-drug exposed/refractory, and 91% refractory to last LOT. AEs in >20% of pts (both iv and sc combined) included anemia (55%), neutropenia (55%), thrombocytopenia (41%), and leukopenia (26%), as well as non-hematologic events of CRS (53%), pyrexia (28%), diarrhea (24%), cough (23%), fatigue (23%), nausea (22%), back pain (20%), and headache (20%). 39% of pts had treatment-related grade ≥3 AEs; neutropenia (23%) and anemia (9%) were most frequent. CRS occurred in 55% and 50% of pts with iv and sc dosing, respectively, tending to occur later (relative to the most recent dose) with sc administration (median time to onset of 1.0 day iv and 2.0 days sc). CRS events were all gr 1 (n=51) or 2 (n=17) and generally confined to initial doses. 5% of pts (all iv) had neurotoxicity (2% gr ≥3), and 12% had treatment-related infusion/injection related reaction (including 4 infusion reactions [all iv, 5%] and 11 injection related reactions [all sc, 25%], all gr 1/2). Gr 3 or higher infection-related AEs were reported in 15% of pts (3% treatment related). Four gr 5 AEs were reported (all iv and considered unrelated to treatment by investigator except for 1 case of pneumonia).

Pharmacokinetic results showed that the half-life of teclistamab supports weekly iv dosing. Exposure increased in an approximately dose-proportional manner following weekly iv or sc treatment dosing. 1500 µg/kg sc dose had comparable C_{max} to that of 270 µg/kg iv and higher trough levels than that of 720 µg/kg iv. Individual time to reach C_{max} following sc dosing ranged from Day 3 – Day 8.

Teclistamab treatment in both iv and sc cohorts led to pharmacodynamic changes supporting mechanism of action, including increases in T cell activation and circulating cytokine levels, such as IL-10, IL-2Ra and IL-6.

120 pts were evaluable for response, with the highest and most active dose levels of 270 µg/kg and 720 µg/kg weekly for iv and 720 µg/kg and 1500 µg/kg weekly for sc (of note, response data for 3000 µg/kg sc is not yet mature). Combining these 4 iv and sc dose levels, ORR was 30/47 (63.8%, including n=24 with very good partial response [VGPR] or better and n=9 with complete response [CR] or better). 1500 µg/kg sc was selected as a RP2D, and currently at this

dose, 6 of 6 pts are in response (3 PR, 1 VGPR, 2 stringent CR) with progressive deepening of responses over time.

Among 48 pts with responses across all iv and sc cohorts, median time to first response was 1 mo (range, 0.3–4.2) and median duration of response has not been reached, with 38 responding pts remaining on therapy 1.6 to 21.3+ months. Of MRD-evaluable pts who had a CR, 4/5 pts treated in the iv cohorts and 2/2 pts in the sc cohorts are MRD negative at 10^{-6}.

Conclusions

Teclistamab has a manageable safety profile, which includes low-grade CRS (with no gr $\geq$3 events) and low severe infection and neurotoxicity rates with both iv and sc administration. Deep and durable responses were observed with both iv and sc administration. The encouraging tolerability and efficacy of teclistamab support the planned phase 2 monotherapy (at 1500 µg/kg sc) trial and future combination studies.