P06 UPDATED RESULTS FROM THE PHASE 1/2 MAJESTEC-1 STUDY OF TECLISTAMAB, A B-CELL MATURATION ANTIGEN X CD3 BISPECIFIC ANTIBODY, IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

Popat, R[1]; Usmani, S[2]; Garfall, A[3]; van de Donk, N[4]; Nahi, H[5]; San-Miguel, J[6]; Oriol, A[7]; Nooka, A[8]; Martin, T[9]; Rosinol, L[10] Chari, A[11]; Karlin, L[12]; Benboubker, L[13]; Mateos, M[14]; Bahlis, N[15]; Moreau, P[16]; Besemer, B[17]; Martínez-López, J[18]; Sidana, S[19]; Pei, L[20]; Trancucci, D[20]; Verona, R[21]; Girgis, S[21]; Olyslager, Y[22]; Jaffe, M[20]; Uhlar, C[21]; Stephenson, T[21]; Van Rampelbergh, R[22]; Banerjee, A[21]; Goldberg, J[20]; Kobos, R[20]; Krishnan, A[23]

[1]University College London Hospitals, NHS Foundation Trust, [2]Levine Cancer Institute/Atrium Health, [3]Abramson Cancer Center, University of Pennsylvania, [4]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, [5]Karolinska University Hospital at Huddinge, [6]Clínica Universidad de Navarra, CIMA, CIBERONC, IDISNA, [7]Institut Català d'Oncologia and Institut Josep Carreras, Hospital Germans Trias i Pujol, [8]Winship Cancer Institute, Emory University, [9]University of California, San Francisco, [10]Hospital Clínic, IDIBAPS, University of Barcelona, [11]Mount Sinai School of Medicine, [12]Service d'Hématologie Clinique, Centre Hospitalier Lyon Sud, [13]Service d'Hématologie et Thérapie Cellulaire, Hôpital Bretonneau, Centre Hospitalier Régional Universitaire, [14]University Hospital of Salamanca/IBSAL/CIC/CIBERONC, [15]Arnie Charbonneau Cancer Institute, University of Calgary, [16]Hematology Clinic, University Hospital Hôtel-Dieu, [17]Department of Hematology, Oncology and Immunology, University of Tuebingen, [18]Haematological Malignancies Clinical Research Unit, Hospital 12 de Octubre Universidad Complutense, CNIO, CIBERONC, [19]Stanford University School of Medicine, [20]Janssen Research & Development, [21]Janssen Research & Development, [22]Janssen Research & Development, [23]City of Hope Comprehensive Cancer Center

Teclistamab (JNJ-64007957) is a bispecific antibody that binds to both B-cell maturation antigen (BCMA) and CD3 receptors to induce T cell-mediated cytotoxicity of BCMA-expressing myeloma cells. Results from phase 1 of the MajesTEC-1 study, an ongoing phase 1/2 study in heavily-pretreated relapsed/refractory multiple myeloma (RRMM; NCT03145181), showed a tolerable safety profile at the recommended phase 2 dose (RP2D) and encouraging efficacy. Here we report initial data from the phase 2 portion of MajesTEC-1 (NCT04557098) as well as updated results from phase 1.

Patients (pts; ≥18 y) had MM per International Myeloma Working Group (IMWG) criteria, 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 (LOT). The primary objectives were to identify the RP2D and to characterize safety and tolerability of teclistamab at the RP2D in phase 1, and to evaluate the efficacy at the RP2D (primary endpoint: ORR) in phase 2. The RP2D was weekly subcutaneous teclistamab 1500 µg/kg following step-up doses of 60 and 300 µg/kg. Responses were assessed by the investigator per IMWG criteria. Adverse events (AEs) were graded per CTCAE v4.03. Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) were graded per ASTCT criteria.

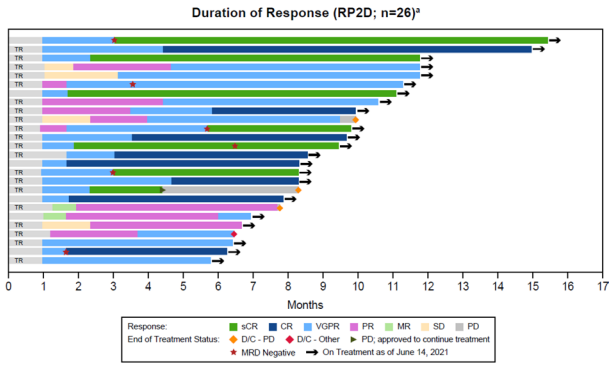
As of June 14, 2021, 159 pts (median age 64.0 y [range 33–84]; 15% ≥75 y; 59% male) were treated at the RP2D (phase 1: 40 pts; phase 2: 119 pts). Pts received a median of 5 prior LOT (range 2–15); 100% were triple-class exposed, 69% were penta-drug exposed, 77% were triple-class refractory, and 29% were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

In 159 pts, the most common nonhematologic AEs at the RP2D were CRS (any grade: 67%; grade 3 occurred in 1 pt, no grade 4 or 5), injection site erythema (23%; all grade 1/2), and fatigue (22%; grade 3/4: 2%). Of the hematologic AEs, most common 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). No new safety signals were identified in phase 2. Phase 2 pharmacokinetic and pharmacodynamic data supported those reported in phase 1. At the RP2D, teclistamab exposure was sustained across the dosing interval and exceeded target exposure levels. Across both phases, induction of proinflammatory cytokines and T cell activation were observed at the RP2D.

Phase 2 efficacy data are immature. At 8.2-mo median follow-up (range 1.2–15.2), responses in the phase 1 pts at the RP2D (n=40) were consistent with previous reports (ORR: 65% [95% CI 48–79]; ≥VGPR: 60% [95% CI 43–75]; ≥complete response: 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). 85% (22/26) of responders are continuing on treatment, including 1 pt with 15.2 mo of follow-up. Median duration of response (DOR) was not reached, with 6-month DOR rate of 90% [95% CI 63–97].

The safety of teclistamab is supported by data from 159 pts treated at the RP2D. Teclistamab continues to show deep and durable responses with a manageable safety profile in heavily-pretreated pts with RRMM.

Figure. Duration of Response



[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

P07 RESULTS FROM THE CC-220-MM-001 DOSE-EXPANSION PHASE OF IBERDOMIDE PLUS DEXAMETHASONE IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

van de Donk, N. W. C. J[1]; Popat, R[2]; Hulin, C[3]; Jagannath, S[4]; Oriol, A[5]; Richardson, P. G[6]; Facon, T[7]; Weisel, K[8]; Larsen, J. T[9]; Minnema, M[10]; Abdallah, A[11]; Badros, A. Z[12]; Knop, S[13]; Stadtmauer, E. A[14]; Chen, M[15]; Nguyen, T. V[15]; Amin, A[15]; Peluso, T[16]; Lonial, S[17]

[1]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Department of Hematology, Cancer Center Amsterdam, Amsterdam, Netherlands; [2]NIHR UCLH Clinical Research Facility, University College London Hospitals NHS Foundation Trust, London, UK; [3]Service d'Hématologie Hôpital Haut-Lévêque, CHU Bordeaux, Pessac, France; [4]The Mount Sinai Hospital, New York, NY, USA; [5]Catalan Institute of Oncology and Josep Carreras Institute, Hospital Germans Trias i Pujol, Badalona, Spain; [6]Dana-Farber Cancer Institute, Boston, MA, USA; [7]Service des Maladies du Sang, CHRU de Lille - Hôpital Claude Huriez, Lille, France; [8]University Medical Center of Hamburg-Eppendorf, Hamburg, Germany; [9]Mayo Clinic Arizona, Phoenix, AZ, USA; [10]University Medical Center Utrecht, Utrecht, Netherlands; [11]University of Kansas Medical Center, Kansas City, KS, USA; [12]Marlene and Stewart Greenebaum Comprehensive Cancer Center, University of Maryland School of Medicine, Baltimore, MD, USA; [13]Medizinische Klinik und Poliklinik II, Universitätsklinikum Würzburg, Würzburg, Germany; [14]University of Pennsylvania, Philadelphia, PA, USA; [15]Bristol Myers Squibb, Princeton, NJ, USA; [16]Celgene International Sàrl, a Bristol-Myers Squibb Company, Boudry, Switzerland; [17]Winship Cancer Institute, Emory University, Atlanta, GA, USA

Iberdomide (IBER), a potent oral cereblon E3 ligase modulator (CELMoD®) agent with enhanced tumoricidal and immune-stimulatory effects versus immunomodulatory (IMiD®) agents, has shown marked synergy with dexamethasone (DEX) and other standard myeloma treatments in preclinical models. IBER is being evaluated with various treatment combinations in patients (pts) with relapsed/refractory multiple myeloma (RRMM) in the phase 1/2 study CC-220-MM-001 (NCT02773030). Results from the dose expansion of IBER+DEX in pts with heavily pretreated, triple-class exposed (≥1 IMiD agent, ≥1 proteasome inhibitor [PI], and ≥1 CD38 monoclonal antibody [mAb]) RRMM are reported here.

Key eligibility criteria were: RRMM; ≥3 prior lines of therapy, including lenalidomide, pomalidomide, a PI, a glucocorticoid, and a CD38 mAb; progressive disease (PD) within 60 days of last myeloma therapy; and refractoriness to an IMiD agent, a PI, a glucocorticoid, and a CD38 mAb. Pts who had received prior anti-BCMA therapy were included in a separate cohort. Oral IBER (at the recommended phase 2 dose of 1.6 mg)