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EFFICACY AND SAFETY OF THE BCMA-DIRECTED CAR-T CELL THERAPY, CILTACABTAGENE AUTOLEUCEL, IN PATIENTS WITH PROGRESSIVE MULTIPLE MYELOMA AFTER 1–3 PRIOR LINES OF THERAPY: INITIAL RESULTS FROM CARTITUDE-2

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Mounzer Agha[1], Adam Cohen[2], Deepu Madduri[3], Yael Cohen[4], Michel Delforge[5], Jens Hillengass[6], Hartmut Goldschmidt[7], Katja Weisel[8], Marc-Steffen Raab[9, 10], Christoph Scheid[11], Jordan Schecter[12], Kevin De Braganca[12], Helen Varsos[12], Liwei Wang[12], Martin Vogel[13], Marlene Carrasco-Alfonso[14], Muhammad Akram[14], Xiaoling Wu[14], Tonia Nesheiwat[14], Hermann Einsele[15]

[1] University of Pittsburgh Medical Center Hillman Cancer Center, Pittsburgh, United States
[2] Abramson Cancer Center, University of Pennsylvania, Philadelphia, United States
[3] Mount Sinai Medical Center, New York, United States
[4] Tel Aviv Sourasky (Ichilov) Medical Center, and Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel
[5] Universitaire Ziekenhuizen Leuven, Leuven, Belgium
[6] Roswell Park Comprehensive Cancer Center, Buffalo, New York, United States
[7] University Hospital Heidelberg, Internal Medicine V and National Center for Tumor Diseases (NCT), Heidelberg, Germany
[8] University Medical Center Hamburg-Eppendorf, Hamburg, Germany
[9] University Hospital Heidelberg, Heidelberg, Germany
[10] Clinical Cooperation Unit Molecular Hematology/Oncology, German Cancer Research Center, Heidelberg, Germany
[11] University of Cologne, Cologne, Germany
[12] Janssen R&D, Raritan, United States
[13] Janssen Global Services, LLC, Raritan, United States
[14] Legend Biotech USA, Inc, Piscataway, United States
[15] Universitätsklinikum Würzburg, Medizinische Klinik und Poliklinik II, Würzburg, Germany

Background: Ciltacabtagene autoleucel (Cilta-cel) is a chimeric antigen receptor T (CAR-T) cell therapy expressing two B-cell maturation antigen (BCMA)-targeting, single-domain antibodies designed to confer avidity. CARTITUDE-2 (NCT04133636) is a multicohort, phase 2 study evaluating cilta-cel safety and efficacy in various clinical settings for patients with multiple myeloma (MM) and exploring suitability of outpatient administration.

Aims: We report initial results from Cohort A of CARTITUDE-2.

Methods: All patients provided informed consent. Patients from Cohort A had progressive MM after 1–3 prior lines of therapy (LOT), including a proteasome inhibitor (PI) and immunomodulatory drug (IMiD), were lenalidomide refractory, and had no prior exposure to BCMA-targeting agents. A single cilta-cel infusion (target dose: 0.75×10^6 CAR+ viable T cells/kg) was given 5–7 days after initiating lymphodepletion (cyclophosphamide [300 mg/m^2] and fludarabine [30 mg/m^2] daily for 3 days). The primary objective was minimal residual disease (MRD) 10^{-5} negativity. Secondary outcomes were response rates per International Myeloma Working Group criteria and safety (adverse events [AEs] were graded per Common Terminology Criteria for Adverse Events; cytokine release syndrome [CRS] and immune effector cell-associated neurotoxicity syndrome [ICANS] were graded per American Society for Transplantation and Cellular Therapy).

Results: At the data cutoff of Feb 2021 (median follow-up of 5.8 months; range: 2.5–9.8), 20 patients (65% male; median age 60 years [range: 38–75]) had received cilta-cel; one patient was treated in an outpatient setting. Patients received a median of 2 prior LOT (range: 1–3); 12 patients received <3 prior LOT and 8 received 3 prior LOT. All patients were exposed to PI, IMiD, and dexamethasone, 95% to alkylating agents, and 65% to

daratumumab. The majority (95%) were refractory to their last LOT, and 40% were triple refractory. The overall response rate was 95% (95% CI: 75–100) with 75% (95% CI: 51–91) achieving ≥complete response, and 85% (95% CI: 62–97) achieving ≥very good partial response. Median time to first response was 1.0 month (range: 0.7–3.3), and median time to best response was 1.9 months (range: 0.9–5.1). The median duration of response was not reached. All patients (n=4) with MRD-evaluable samples at 10^{-5} at the time of data cutoff were MRD-negative. Hematologic AEs (in ≥20% of patients) were neutropenia (95%; grade 3/4: 90%), thrombocytopenia (80%; grade 3/4: 35%), anemia (65%; grade 3/4: 40%), lymphopenia (60%; grade 3/4: 55%), and leukopenia (55%; all grade 3/4). CRS occurred in 85% of patients; 10% were grade 3/4. The median time to CRS onset was 7 days (range: 5–9), with a median duration of 3.5 days (range: 2–11). CAR-T cell neurotoxicity occurred in 20% of patients (all grade 1/2). Three patients had ICANS (1 was grade 1; 2 were grade 2) with median time to onset of 8 days (range: 7–11) and median duration of 2 days (range: 1–2). One patient had grade 2 facial paralysis with time to onset of 29 days and duration of 51 days. One death occurred due to COVID-19, which was assessed as treatment-related by investigator. The safety profile was manageable in the patient treated in an outpatient setting.

Summary/Conclusion: A single cilta-cel infusion at the recommended phase 2 dose led to early and deep responses with manageable safety in patients with MM who had received 1–3 prior LOT. Updated efficacy and safety findings will inform suitability of outpatient treatment in this and other cohorts of CARTITUDE-2 as well as the CARTITUDE-4 study.

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