## UPDATED RESULTS FROM THE CARTITUDE-1 STUDY OF CILTACABTAGENE AUTOLEUCEL, A B-CELL MATURATION ANTIGEN–DIRECTED CHIMERIC ANTIGEN RECEPTOR T CELL THERAPY, IN RELAPSED/REFRACTORY MULTIPLE MYELOMA

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**Objectives:** CARTITUDE-1 (NCT03548207) is a phase 1b/2 study of ciltacabtagene autoleucel (cilta-cel; JNJ-68284528), a chimeric antigen receptor T cell (CAR-T) therapy with two B-cell maturation antigen (BCMA)–targeting single-domain antibodies, in relapsed/refractory multiple myeloma (RRMM). Updated results from a median 18-month follow-up are reported here. **Material and methods:** Eligible patients had MM, received ≥3 prior regimens or were double refractory to a proteasome inhibitor (PI) and immunomodulatory drug (IMiD), and had received a PI, IMiD, and anti-CD38 antibody. After apheresis, bridging therapy was allowed. Patients received a single cilta-cel infusion (target dose: $0.75\times10^6$ CAR + viable T cells/kg; range $0.5\text{-}1.0\times10^6$) 5–7 days (d) after lymphodepletion (300 mg/m$^2$ cyclophosphamide, 30 mg/m$^2$ fludarabine daily for 3 d). Primary objectives were to characterize cilta-cel safety, confirm the recommended phase 2 dose (phase 1b), and evaluate efficacy (phase 2). Cytokine release syndrome (CRS) was graded by Lee *et al* (Blood 2014) and neurotoxicity by CTCAE, v5.0 in phase 1b. CRS and immune effector cell-associated neurotoxicity syndrome (ICANS) were graded by American Society for Transplantation and Cellular Therapy (ASTCT) criteria in phase 2. Lee et al and CTCAE v5.0 were mapped to ASTCT for CRS and ICANS, respectively. **Results:** As of February 11, 2021, 97 patients (median of 6 prior lines) received cilta-cel. Overall response rate per independent review committee (primary endpoint) was 97.9% (95% CI, 92.7–99.7); 80.4% achieved stringent complete response (sCR) and 94.8% achieved very good partial response or better. Median time to first response was 1 month (mo) (range, 0.9–10.7), and median time to ≥CR was 2.6 mo (range, 0.9–15.2). Median duration of response was 21.8 mo (95% CI, 21.8–NE). Of 61 minimal residual disease (MRD)-evaluable patients, 91.8% were MRD negative at $10^{-5}$. The 18-month progression-free survival (PFS) and overall survival rates (95% CI) were 66% (54.9–75.0) and 80.9% (71.4–87.6), respectively; median PFS was 22.8 mo (95% CI, 22.8–NE) for all patients, and not reached for patients with sCR. Grade 3/4 hematologic AEs ≥20% included neutropenia (95%), anemia (68%), leukopenia (61%), thrombocytopenia (60%), and lymphopenia (50%). CRS occurred in 95% of patients (4% grade 3/4); median time to onset was 7 d (range, 1–12) and median duration was 4 d (range, 1–14, excluding 1 patient with 97-d duration). CRS resolved in all but one with grade 5 CRS/hemophagocytic lymphohistiocytosis. 21% of patients had CAR-T neurotoxicity (grade ≥3, 10%). Twenty-one deaths occurred during the study: none ≤30 days; 2 ≤100 days; and 19 >100 days after infusion, among which, 10 were due to disease progression, 6 were treatment-related as assessed by the investigator, and 5 were due to AEs unrelated to treatment. **Discussion:** Cilta-cel is under further investigation in other MM populations in earlier lines of therapy and in outpatient settings. **Conclusions:** At a longer median follow-up of 18 mo, a single cilta-cel infusion yielded early, deep, and durable responses with a manageable safety, in heavily pretreated patients with MM.

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## USING A NONVIRAL AND NONINTEGRATING DNA VECTOR TO GENERATE SAFE CAR-T CELLS

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**Aims:** CAR-T cell therapy has proven its importance in cancer treatment and currently there are five approved products on the market. However, these products are based on viral vectors, which presents a risk of insertional mutagenesis, it can also be immunogenic and its manufacture is extremely expensive. The development of a nonviral vector, suitable for