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CARTITUDE-1: Phase 1b/2 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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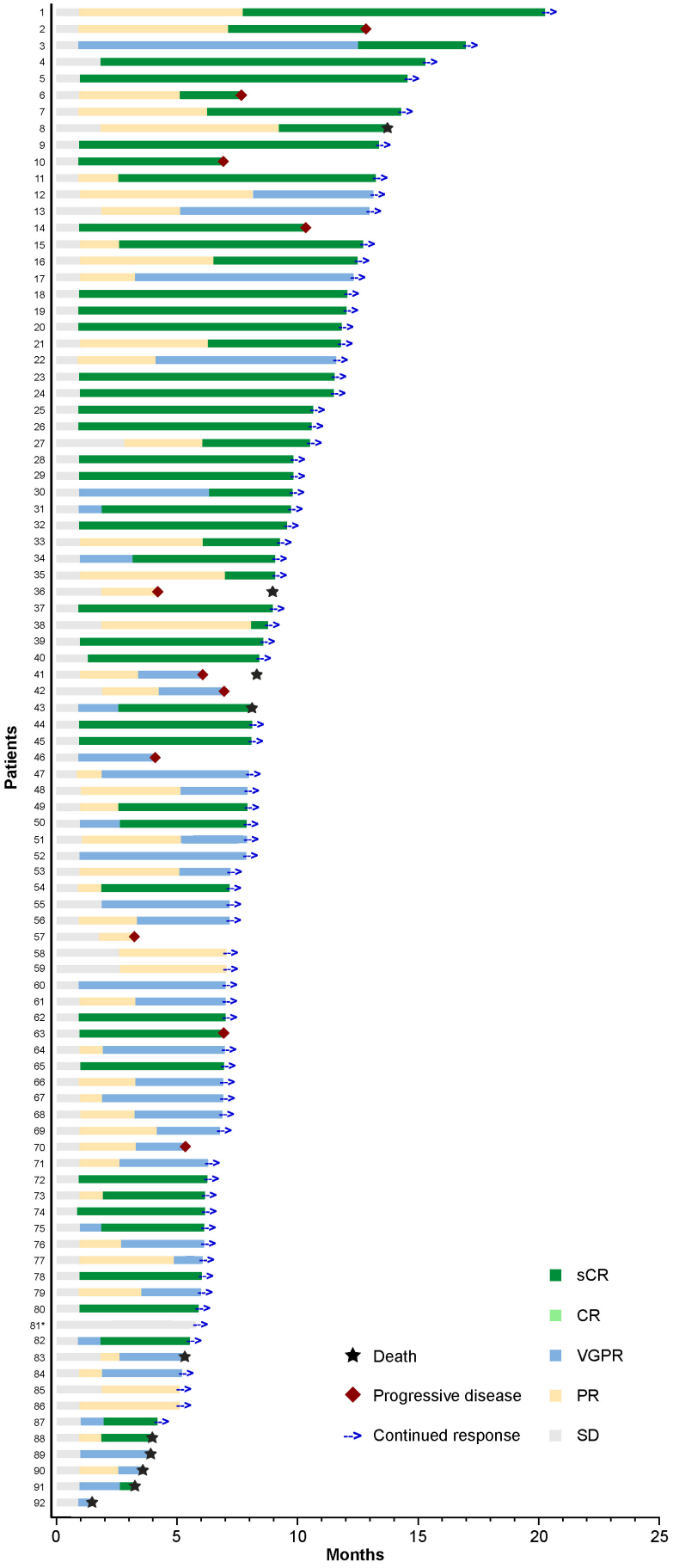
Background: Ciltacabtagene autoleucel (cilta-cel; JNJ-68284528; LCAR-B38M CAR-T cells) is a chimeric antigen receptor T (CAR-T) cell therapy with 2 B-cell maturation antigen–targeting single-domain antibodies designed to confer avidity. In the phase 1 LEGEND-2 study in China, LCAR-B38M yielded deep, durable responses with a manageable safety profile in patients (pts) with relapsed/refractory multiple myeloma (R/R MM). The phase 1b/2 CARTITUDE-1 study (NCT03548207) is further evaluating cilta-cel in this pt population in the US. We present updated data from the phase 1b portion along with initial phase 2 data.

Methods: Eligible pts (aged ≥18 y) were diagnosed with MM per International Myeloma Working Group (IMWG) criteria and had measurable disease, Eastern Cooperative Oncology Group performance status ≤1, received ≥3 prior regimens or were double-refractory to a proteasome inhibitor and immunomodulatory drug, and received an anti-CD38 antibody. After apheresis, bridging therapy was permitted. Cyclophosphamide 300 mg/m^2 and fludarabine 30 mg/m^2 daily for 3 d were used for lymphodepletion. A single infusion of cilta-cel at a target dose of 0.75×10^6 (range $0.5–1.0\times10^6$) CAR+ viable T cells/kg was administered 5–7 d after start of lymphodepletion. The primary objective of the phase 1b portion was to characterize cilta-cel safety and establish the recommended phase 2 dose; the primary objective of the phase 2 portion was to evaluate cilta-cel efficacy. Response was assessed per IMWG criteria and minimal residual disease (MRD) by next-generation sequencing. Adverse events (AEs) were graded using CTCAE v5.0. In the phase 1b portion, cytokine release syndrome (CRS) was graded by Lee et al (*Blood* 2014) and neurotoxicity by CTCAE v5.0; in the phase 2 portion, CRS and neurotoxicity were graded by American Society for Transplantation and Cellular Therapy (ASTCT) criteria. In this combined analysis, Lee et al and CTCAE v5.0 were mapped to ASTCT criteria for CRS and immune effector cell-associated neurotoxicity syndrome (ICANS), respectively.

Results: As of the May 20, 2020 clinical cutoff, 97 pts (58.8% male; median age 61.0 y [range 43–78]) with R/R MM received cilta-cel (29 in phase 1b; 68 in phase 2). Median follow-up duration was 8.8 mo (range 1.5–20.4). Pts had received a median of 6 prior lines of therapy (range 3–18); 83.5% were penta-exposed, 87.6% were triple-refractory, 41.2% were penta-refractory, and 97.9% were refractory to last line of therapy. Overall response rate per independent review committee (primary endpoint) was 94.8% (95% CI 88.4–98.3), with a stringent complete response rate of 55.7% (95% CI 45.2–65.8), very good partial response rate of 32.0% (95% CI 22.9–42.2), and partial response rate of 7.2% (95% CI 3.0–14.3). All pts achieved a reduction in M-protein. Median time to first response was 1.0 mo (range 0.9–5.8; 80.4% ≤1.0 mo), and median time to complete response or better was 1.8 mo (range 0.9–12.5; 74.1% ≤3.0 mo); responses deepened over time (**Figure**). Median duration of response was not reached (NR). Of 52 MRD-evaluable pts, 94.2% were MRD-negative at 10^{-5}. The 6-mo progression-free survival (PFS) and overall survival (OS) rates (95% CI) were 87.4% (78.9–92.7) and 93.8% (86.7–97.2), respectively; median PFS and OS were NR. Ten deaths occurred during the study; 8 were due to AEs (both related and unrelated; CRS/hemophagocytic lymphohistiocytosis, neurotoxicity, respiratory failure, sepsis, septic shock, pneumonia, lung abscess, and acute myelogenous leukemia [n=1 each]), and 2 due to progressive disease. AEs reported in >70% of pts were CRS (94.8%; grade [gr] 3/4 4.1%), neutropenia (90.7%; gr 3/4 90.7%), anemia (81.4%; gr 3/4 68.0%), and thrombocytopenia (79.4%; gr 3/4 59.8%). Median time to CRS onset was 7.0 d (range 1–12) and median duration 4.0 d (range 1–27, excluding n=1 with 97 d). CAR-T cell–related neurotoxicity was reported in 20.6% of pts (gr 3/4 10.3%). Cilta-cel CAR+ T cells showed maximum peripheral expansion at 14 d (range 9–43). Among pts with 6 mo' individual follow-up, 67% had cilta-cel CAR+ T cells below the level of quantification (2 cells/μL) in peripheral blood.

Conclusions: Preliminary phase 1b/2 data from CARTITUDE-1 indicate a single low-dose infusion of cilta-cel leads to early, deep, and durable responses in heavily pretreated pts with MM with a safety profile consistent with LEGEND-2. Further investigation of cilta-cel in other MM populations is underway.

Figure. Duration of response (n=92).



*First response date was the same as the last disease evaluation date.
CR=complete response; PR=partial response; sCR=stringent complete response; SD=stable disease; VGPR=very good partial response.

Disclosures:

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