Patient Identification for Chimeric Antigen Receptor T-Cell Therapy: Initial Insights From the CARTITUDE Program in Multiple Myeloma

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INTRODUCTION

- Previous studies of chimeric antigen receptor T-cell (CAR T) therapies for multiple myeloma (MM) have primarily included patients with heavily pretreated or refractory disease[1,2]
- Ciltacabtagene autoleucel (cilta-cel) is a B-cell maturation antigen (BCMA)-directed CAR-T therapy being developed for the treatment of MM[1,3]
- The CARTITUDE clinical trial program was designed to investigate the safety and efficacy of cilta-cel in various patient populations with MM, including patients with newly diagnosed MM for whom early CAR-T therapy may provide deep and durable benefit

OBJECTIVE

- To describe the patient populations included in the CARTITUDE clinical trial program

METHODS

- In all CARTITUDE trials, inclusion criteria include adults with MM and Eastern Cooperative Oncology Group (ECOG) Performance Status grade ≤1; trial-specific eligibility criteria are shown in **Figure 1**
- CARTITUDE-1 and -2 were single-arm studies in which participants received cilta-cel infusion with a target dose of 0.75 × 10^6 CAR-positive viable T cells/kg
  - CARTITUDE-2 is a multicohort study that includes participants with relapsed/refractory MM and newly diagnosed MM
- CARTITUDE-4 and -5 are randomized trials comparing cilta-cel infusion with current standard-of-care therapy
- The current analysis is focused on the patient populations included in CARTITUDE-1 and Cohorts A and B from CARTITUDE-2

FIGURE 1: Cilta-cel program overview[a]

	Relapsed/Refractory MM			Newly diagnosed MM	
	CARTITUDE-1	CARTITUDE-2[b]	CARTITUDE-4	CARTITUDE-2[b]	CARTITUDE-5
Trial Information	Phase 1b/2 Single arm NCT03548207	Phase 2 Single arm NCT04133636	Phase 3 Randomized NCT04181827	Phase 2 Single arm NCT04133636	Phase 3 Randomized NCT04923893
Key Eligibility Criteria	• ≥3 prior lines of therapy or double refractory to an IMiD and PI • Measurable disease at screening • Received PI, IMiD, and anti-CD38 • No prior CAR-T therapy or BCMA-targeting therapy • Progressive disease on or within 12 months of last line of therapy	• **Cohort A:** 1-3 prior lines of therapy (PI and IMiD) and lenalidomide refractory; no prior CAR-T or BCMA-targeting therapy • **Cohort B:** 1 prior line of therapy (PI and IMiD); disease progression ≤12 months after ASCT or start of therapy; no prior CAR-T or **BCMA-targeting therapy** • **Cohort C:** Prior treatment with PI, IMiD, anti-CD38, and prior BCMA-targeting therapy; no prior cellular immunotherapy	• 1-3 prior lines of therapy (IMiD and PI) • Refractory to lenalidomide • Disease progression within 36 months of stem cell transplant or 42 months of starting initial therapy (if only 1 prior line of therapy) • No prior CAR-T therapy or BCMA-targeting therapy	• **Cohort D:** Newly diagnosed MM; <CR after ASCT with or without consolidation; no prior CAR-T or BCMA-targeted therapy • **Cohort E:** Newly diagnosed MM without prior therapy; high-risk disease; ASCT not planned • **Cohort F:** Newly diagnosed MM with 4-8 cycles initial therapy and ≥VGPR response; standard risk; no prior CAR-T, BCMA-targeted therapy, or stem cell transplant	• Newly diagnosed MM and not considered for high-dose chemotherapy with ASCT • No prior CAR-T therapy or BCMA-targeting therapy • No prior therapy for MM or smoldering myeloma other than a short course of corticosteroids or a maximum 1 cycle of VRd therapy prior to enrollment
Treatments	Cilta-cel infusion	Cilta-cel infusion	Cilta-cel infusion vs standard of care	**Cohort D:** Cilta-cel infusion ± lenalidomide **Cohort E:** Cilta-cel infusion + VRd + daratumumab **Cohort F:** Cilta-cel infusion	Cilta-cel infusion vs standard of care

ASCT, autologous stem cell transplantation; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; CR, complete response; DVRd, daratumumab, bortezomib, lenalidomide, and dexamethasone; IMiD, immunomodulatory drug; MM, multiple myeloma; NDMM, newly diagnosed MM; PI, proteasome inhibitor; RRMM, relapsed/refractory MM; VGPR, very good partial response; VRd, bortezomib, lenalidomide, and dexamethasone. [a]An additional phase 3 randomized trial comparing DVRd followed by cilta-cel vs DVRd followed by ASCT in patients with NDMM is also ongoing (CARTITUDE-6; NCT05257083). [b]CARTITUDE-2 is composed of 6 total cohorts; 3 cohorts include patients with RRMM, and 3 cohorts include patients with NDMM.

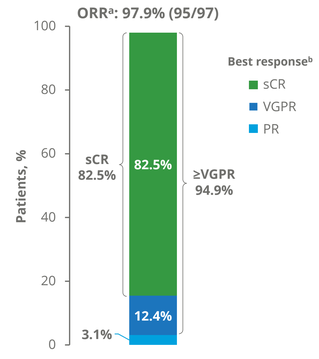
MULTIPLE MYELOMA

RESULTS

CARTITUDE-1 Results

- Data from the phase 1b/2 CARTITUDE-1 study demonstrating early, deep, and durable responses in heavily pretreated participants with relapsed/refractory multiple myeloma (RRMM) has been previously reported[1]
- The overall response rate (ORR) after a median ~2 years of follow-up after CARTITUDE-1 is shown in **Figure 2**
- Over the follow-up period (median ~2 years), no new safety signals (including no new movement and neurocognitive treatment-emergent adverse events [MNTs]) were observed with respect to the median ~1-year follow-up
- Patient management strategies were implemented during CARTITUDE-1; after implementation of these strategies, approximately 200 additional patients have received cilta-cel across the CARTITUDE clinical program; and the overall incidence of MNTs has decreased from 5% to 0.5% as of October 2021

FIGURE 2: CARTITUDE-1 efficacy response[3]

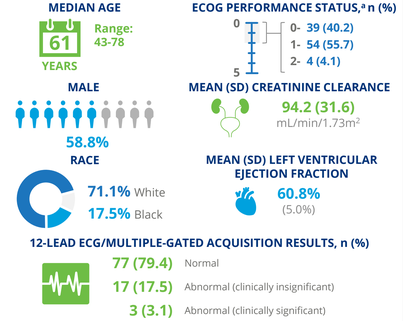


ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response. Median follow-up was 21.7 months with data cut-off of July 22, 2021. [a]ORR assessed by independent review committee. [b]No patient had CR or stable disease as best response.

CARTITUDE-1 Baseline Characteristics

- Baseline demographics and clinical characteristics of participants in CARTITUDE-1 are shown in **Figure 3**
- Participant baseline clinical characteristics and commonly reported prior comorbidities in CARTITUDE-1 are summarized in **Tables 1** and **2**, respectively

FIGURE 3: CARTITUDE-1 participant demographics and baseline characteristics



[a]All participants met the inclusion criteria of ECOG performance score of 0 or 1 during screening. ECG, electrocardiogram; ECOG, Eastern Cooperative Oncology Group.

TABLE 1: Additional CARTITUDE-1 participant baseline characteristics and treatment history

Characteristics	N=97
All plasmacytomas[a], n (%)	19 (19.6)
Extramedullary plasmacytomas	13 (13.4)
Bone-based plasmacytomas	6 (6.2)
High-risk cytogenetic profile, n (%)	23 (23.7)
Prior lines of therapy, median (range)	6.0 (3-18)
Triple-class exposed,[b] n (%)	97 (100.0)
Triple-class refractory,[b] n (%)	85 (87.6)
Penta-drug exposed,[c] n (%)	81 (83.5)
Penta-drug refractory,[c] n (%)	41 (42.3)
Refractory to last line of therapy, n (%)	96 (99.0)

BCMA, B-cell maturation antigen; IMiD, immunomodulatory drug; PI, proteasome inhibitor. [a]The number of evaluable samples was 62; BCMA expression detected in all evaluable samples. [b]≥1 PI, ≥1 IMiD, and 1 anti-CD38 antibody. [c]≥2 PIs, ≥2 IMiDs, and 1 anti-CD38 antibody.

TABLE 2: CARTITUDE-1 participant ongoing medical conditions (≥45% of participants)

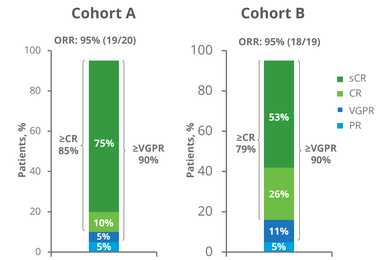
Comorbidity[a]	n (%)
Any	96 (99)
Peripheral sensory neuropathy	60 (61.9)
Fatigue	53 (54.6)
Anemia	48 (49.5)
Hypertension	44 (45.4)

[a]Medical history is reported using MeDRA version 23.0.

CARTITUDE-2 ORR

- The ORR for Cohorts A and B is shown in **Figure 4**

Figure 4. Overall response rate in CARTITUDE-2 Cohorts A and B[4,5]



CR, complete response; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

CARTITUDE-2 Baseline Characteristics

- To date, participant baseline characteristics are available for CARTITUDE-2 Cohorts A and B (**Table 3**)
  - Baseline clinical characteristics of participants in Cohorts A and B were consistent with study inclusion criteria
  - In Cohorts A and B, 40% and 16% of participants were triple-class refractory at baseline, respectively

TABLE 3: CARTITUDE-2 baseline characteristics (Cohorts A and B)

Characteristic	Cohort A (n=20)	Cohort B (n=19)
Age, y, median (range)	60 (38-75)	58 (44-67)
Male, n (%)	13 (65.0)	14 (73.7)
Extramedullary plasmacytomas, n (%)	3 (15.0)	2 (10.5)
High-risk cytogenetic profile, n (%)	7 (35.0)	3 (15.8)
Prior lines of therapy, median (range)	2 (1-3)	1 (1-1)
Triple-class exposed,[a] n (%)	13 (65.0)	4 (21.1)
Triple-class refractory,[a] n (%)	8 (40.0)	3 (15.8)
Penta-drug exposed,[b] n (%)	4 (20.0)	0 (0)
Penta-drug refractory,[b] n (%)	1 (5.0)	0 (0)
Refractory to last line of therapy, n (%)	19 (95.0)	15 (78.9)

IMiD, immunomodulatory drug; PI, proteasome inhibitor. [a]≥1 PI, ≥1 IMiD, and 1 anti-CD38 antibody. [b]≥2 PIs, ≥2 IMiDs, and 1 anti-CD38 antibody.

KEY TAKEAWAYS

Current and future data from the CARTITUDE trials will aid characterization of patients with MM who may benefit from CAR-T therapy

CONCLUSIONS

Participants in CARTITUDE-1 had generally good functional status and adequate renal and cardiac function

Studies assessing the safety and efficacy of cilta-cel in participants with MM in earlier-line settings and in newly diagnosed MM are currently ongoing

Monitoring of real-world patient characteristics now that cilta-cel is commercially available will be important to identify physicians' prescribing preferences

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DISCLOSURES

ISM has received consultancy fees from Janssen Pharmaceuticals, Inc. LB and DM are employed by Janssen Pharmaceuticals, Inc.

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