Efficacy Outcomes and Characteristics of Patients With Multiple Myeloma Who Achieved Sustained Minimal Residual Disease Negativity After Treatment With Ciltacabtagene Autoleucel in CARTITUDE-1

Nikhil C Munshi,[1] Bruno Paiva,[2] Thomas Martin,[3] Saad Z Usmani,[4] Yi Lin,[5] Jordan M Schecter,[6] Carolyn C Jackson,[6] Deepu Madduri,[6] Enrique Zudaire,[7] Tzu-Min Yeh,[6] J Blake Bartlett,[8] Lida Pacaud,[9] Muhammad Akram,[9] Dong Geng,[9] Sundar Jagannath,[10] Adam D Cohen,[11] Jesús San-Miguel[2]

[1]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, US, and VA Boston Healthcare System, West Roxbury, MA, US; [2]University of Navarra, Pamplona, Spain; [3]UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Mayo Clinic, Rochester, MN, US; [6]Janssen Research & Development, Raritan, NJ, US; [7]Janssen Research & Development, Spring House, PA, US; [8]Janssen Research & Development, Bridgewater, NJ, US; [9]Legend Biotech USA Inc., Piscataway, NJ, US; [10]Mount Sinai Medical Center, New York, NY, US; [11]Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, US

INTRODUCTION

- Ciltacabtagene autoleucel (cilta-cel) is a B-cell maturation antigen (BCMA)-targeting chimeric antigen receptor (CAR)-T cell therapy that was recently approved by the US Food and Drug Administration for the treatment of adult patients with relapsed/refractory multiple myeloma (RRMM) after ≥4 prior lines of therapy (LOT)[1,2]
- In the phase 1b/2 CARTITUDE-1 study, cilta-cel demonstrated deep and durable responses in heavily pretreated patients (median 6 prior LOT) with RRMM at a median follow-up of 28 months[3]
  - The overall response rate (ORR) was 97.9%
  - Median duration of response (DOR) and progression-free survival (PFS) were not reached
  - Of the 97 patients who received cilta-cel, 61 were evaluable for minimal residual disease (MRD) negativity, and 56 (91.8%) achieved MRD negativity (10-5 threshold) at any point
- In this analysis, we report the baseline characteristics and treatment outcomes of patients with sustained MRD negativity

METHODS

CARTITUDE-1 study design and patients

- Eligible patients had a confirmed multiple myeloma (MM) diagnosis, received ≥3 prior therapies or were refractory to a proteasome inhibitor (PI) and immunomodulatory drug (IMiD), and had received a PI, an IMiD, and an anti-CD38 monoclonal antibody
- Patients received a single cilta-cel infusion at a target dose of 0.75×10^6 CAR+ viable T cells/kg 5–7 days after the start of lymphodepletion
- MRD negativity was a key secondary endpoint of the phase 2 portion of CARTITUDE-1

Assessment of MRD negativity

- MRD negativity (10^{-5} threshold) was assessed on bone marrow samples using next-generation sequencing (clonoSEQ v2.0, Adaptive Biotechnologies), regardless of conventional response determination by International Myeloma Working Group criteria at baseline, on day 28, and at 6, 12, 18, and 24 months post cilta-cel infusion
  - An additional sample was collected and assessed at the time of suspected complete response (CR) and every 12 months until progressive disease (PD) for patients who remained on study
  - Evaluable samples passed calibration and quality control and included sufficient cells for evaluation at a testing threshold of 10^{-5}
- Patients with sustained MRD negativity were defined as those who had 2 MRD-negative results after cilta-cel infusion and prior to progression or subsequent therapy that were ≥6 months apart, without any MRD-positive results in between
- Patients who did not achieve MRD negativity at any time point were considered MRD positive
- Landmark analyses were conducted at 6 and 12 months to address immortal time bias

MULTIPLE MYELOMA

RESULTS

MRD negativity in CARTITUDE-1

- Of the 61 patients evaluable for MRD, 56 (91.8%) patients achieved MRD negativity
- MRD negativity was sustained for <6 months in 22 patients, 6–12 months in 10 patients, and ≥12 months in 24 patients

Characteristics of patients with sustained MRD negativity

- Potential associations between patient characteristics and sustained MRD negativity were analyzed descriptively (**Table**)
  - Patients with sustained MRD negativity for ≥12 months had a trend toward a longer time since diagnosis
  - Other baseline characteristics did not vary across MRD subgroups and were similar to those of the overall CARTITUDE-1 population[3]

Efficacy outcomes in MRD subgroups

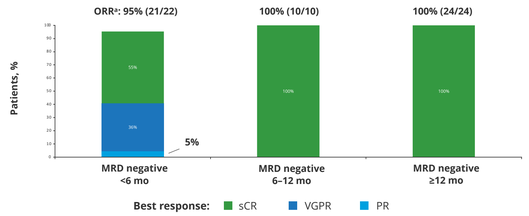
- All patients with sustained MRD negativity for ≥6 months achieved stringent CR (sCR; **Figure 1**)
- Patients with sustained MRD negativity had longer DOR and PFS compared with those who did not (**Figure 2**), consistent with results from landmark analyses[3]
  - The small number of patients in the MRD-positive group (n=5; **Supplemental Figure**) prevents comparisons with those who achieved MRD negativity

TABLE: Baseline characteristics in MRD subgroups

Characteristic	MRD negative <6 months (n=22)	Sustained MRD negative (n=34)	
		6–12 months (n=10)	≥12 months (n=24)
Age, median (range), y	59.5 (51–75)	66.0 (54–77)	63.0 (43–78)
Female, n (%)	8 (36.4)	6 (60.0)	13 (54.2)
Race, n (%)			
White	17 (77.3)	7 (70.0)	14 (58.3)
Black	4 (18.2)	2 (20.0)	4 (16.7)
Time since diagnosis, median (range), y	4.8 (1.6–16.3)	5.0 (1.6–8.1)	7.0 (2.5–18.2)
Plasmacytomas, n (%)	6 (27.3)	2 (20)	2 (8.3)
Extramedullary	4 (18.2)	2 (20)	1 (4.2)
Bone-based	2 (9.1)	0	1 (4.2)
High-risk cytogenetic profile, n (%)	6 (27.3)	2 (20)	6 (25.0)
ECOG performance status at screening, n (%)			
0	10 (45.5)	4 (40.0)	12 (50.0)
1	10 (45.5)	6 (60.0)	12 (50.0)
2	2 (9.1)	0	0
International Staging System stage, n (%)			
I	15 (68.2)	5 (50.0)	18 (75.0)
II	6 (27.3)	2 (20.0)	4 (16.7)
III	1 (4.5)	3 (30.0)	2 (8.3)
Tumor BCMA expression ≥50%, n/N (%)	14/14 (100)	4/6 (66.7)	16/18 (88.9)
Previous stem cell transplant, n (%)			
Autologous	19 (86.4)	6 (60.0)	22 (91.7)
Allogeneic	1 (4.5)	0	2 (8.3)
No. of prior LOT for MM, median (range)	5.0 (3–18)	4.5 (3–12)	5.5 (3–11)
Triple-class refractory,[a] n (%)	21 (95.5)	8 (80.0)	21 (87.5)
Penta-drug exposed,[b] n (%)	18 (81.8)	7 (70.0)	19 (79.2)
Penta-drug refractory,[b] n (%)	6 (27.3)	4 (40.0)	7 (29.2)
Refractory to last LOT, n (%)	22 (100)	10 (100)	24 (100)

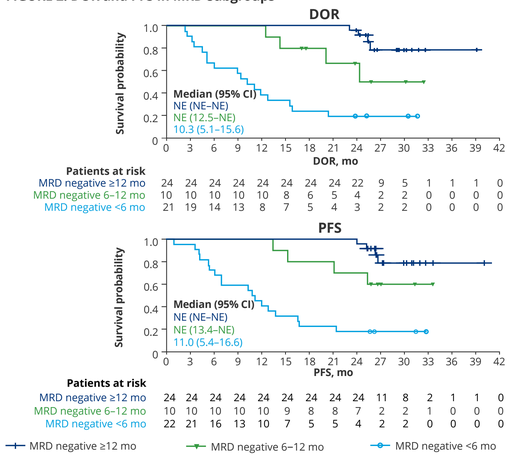
[a]≥1 PI, ≥1 IMiD, and 1 anti-CD38 antibody. [b]≥2 PIs, ≥2 IMiDs, and 1 anti-CD38 antibody. ECOG, Eastern Cooperative Oncology Group.

FIGURE 1: Response to cilta-cel in MRD subgroups



[a]ORR = sCR + CR + VGPR + PR; may not sum appropriately as shown due to rounding. PR, partial response; VGPR, very good partial response.

FIGURE 2: DOR and PFS in MRD subgroups



REFERENCES:

1. Berdeja JG, et al. *Lancet.* 2021; 398:314-24. **2.** CARVYKTI® (ciltacabtagene autoleucel). Prescribing information. Janssen Biotech, Inc.; 2022. **3.** Martin T, et al. *J Clin Oncol.* Published online June 4, 2022. doi: 10.1200/JCO.22.00842.

Presented at the 11th Society of Hematologic Oncology (SOHO) Annual Meeting; September 6-9, 2023; Houston, TX, US & Virtual

KEY TAKEAWAY

Achievement of sustained MRD negativity (≥6 months) resulted in longer DOR and PFS compared with MRD negativity sustained for <6 months

CONCLUSIONS

Baseline patient and disease characteristics did not predict achievement of sustained MRD negativity, but patients with sustained MRD negativity ≥12 months descriptively tended to have a longer time since diagnosis

Patients who achieved sustained MRD negativity for ≥6 months had deeper responses than those with MRD negativity sustained for <6 months

ACKNOWLEDGMENTS

This study was funded by Janssen Research & Development, LLC, and Legend Biotech USA Inc. Medical writing support was provided by MedThink SciCom and funded by Janssen Global Services, LLC.

This poster has been previously presented at the American Society of Hematology (ASH) 2022 Hybrid Congress; New Orleans, LA, US.

DISCLOSURES

NCM has served in a consulting role for AbbVie, Adaptive Biotechnologies, Amgen, BMS, Celgene, GSK, Janssen, Karyopharm, Legend Biotech USA Inc., Novartis, Oncopeptides, Pfizer, and Takeda Oncology; and is a current equity holder in, scientific founder of, and recipient of patents and royalties from Oncopeptides. **BP** has received honoraria from Adaptive Biotechnologies, Amgen, BMS, Gilead, GSK, Janssen, Oncopeptides, Roche Glycart AG, Sanofi, and Takeda; has received research funding from BMS, EngMab, GSK, Roche Glycart AG, Sanofi, and Takeda; and has served in a consulting role for BMS, Janssen, and Sanofi. **TM** has received research funding from Amgen, Janssen, Sanofi, and Seattle Genetics; and has served in a consulting role for GSK, Juno, and Roche. **SZU** has received research funding from Amgen, Array Biopharma, BMS, Celgene, GSK, Janssen, Merck, Pharmacyclics, Sanofi, Seattle Genetics, SkylineDx, and Takeda; has served in a consulting role for AbbVie, Amgen, BMS, Celgene, EdoPharma, Genentech, Gilead, GSK, Janssen, Oncopeptides, Sanofi, Seattle Genetics, Secura Bio, SkylineDx, Takeda, and TeneoBio; and has served on speakers' bureaus for Amgen, BMS, Janssen, and Sanofi. **YL** has served in a consulting role for Bluebird Bio, Celgene, Gamida Cell, Janssen, Novartis, Juno, Kite (a Gilead Company), Legend Biotech USA Inc., Sorrento, and Vineti; and has received research funding from Bluebird Bio, Celgene, Janssen, Kite (a Gilead company), Merck, and Takeda. **JMS** and **JBB** are employees of and own stock in Janssen. **CCJ**, **EZ**, and **T-MY** are employees of Janssen. **DM** is an employee of Janssen; has served in a consulting role for BMS, Celgene, GSK, Kinevant, Legend Biotech USA Inc., Sanofi, and Takeda; and has received research funding from Allogene, Amgen, BMS, and Celgene. **LP**, **MA**, and **DG** are employees of Legend Biotech USA Inc. **SJ** has served in a consulting role for BMS, Legend Biotech USA Inc., Janssen, Karyopharm, Sanofi, and Takeda. **ADC** has served in a consulting/advisory role for AstraZeneca, BMS, Celgene, GSK, Ichnos, Janssen, Oncopeptides, Pfizer, Seattle Genetics, Genentech/Roche, and Takeda; has received research funding from GSK and Novartis; and has received patents and royalties from Novartis. **JS-M** has served in a consulting/advisory role for AbbVie, Amgen, BMS, Celgene, GSK, Haemalogix, Janssen-Cilag, Karyopharm, MSD, Novartis, Takeda, Regeneron, Roche, Sanofi, and Secura Bio.