CARTITUDE-1 Final Results: Phase 1b/2 Study of Ciltacabtagene Autoleucel in Heavily Pretreated Patients With Relapsed/Refractory Multiple Myeloma

Yi Lin,[1] Thomas G Martin,[2] Saad Z Usmani,[3] Jesus G Berdeja,[4] Andrzej J Jakubowiak,[5] Mounzer E Agha,[6] Adam D Cohen,[7] Abhinav Deol,[8] Myo Htut,[9] Alexander M Lesokhin,[3] Nikhil C Munshi,[10] Elizabeth O'Donnell,[11] Carolyn C Jackson,[12] Tzu-Min Yeh,[12] Arnob Banerjee,[13] Enrique Zudaire,[13] Deepu Madduri,[12] Christopher delCorral,[14] Lida Pacaud,[14] Sundar Jagannath[15]

[1]Mayo Clinic, Rochester, MN, US; [2]University of California, San Francisco, San Francisco, CA, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Sarah Cannon Research Institute, Nashville, TN, US; [5]University of Chicago, Chicago, IL, US; [6]UPMC Hillman Cancer Center, Pittsburgh, PA, US; [7]Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, US; [8]Karmanos Cancer Institute, Wayne State University, Detroit, MI, US; [9]City of Hope Comprehensive Cancer Center, Duarte, CA, US; [10]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, US, and VA Boston Healthcare System, West Roxbury, MA, US; [11]Massachusetts General Hospital, Harvard Medical School, Boston, MA, US; [12]Janssen Research & Development, Raritan, NJ, US; [13]Janssen Research & Development, Spring House, PA, US; [14]Legend Biotech USA Inc., Somerset, NJ, US; [15]Mount Sinai Medical Center, New York, NY, US

INTRODUCTION

- Ciltacabtagene autoleucel (cilta-cel) is a dual-binding, B-cell maturation antigen (BCMA), chimeric antigen receptor (CAR)-T cell therapy for the treatment of patients with relapsed/refractory multiple myeloma (RRMM)[1,2]
  - Heavily pretreated patients with RRMM who are treated with standard-of-care therapy have a median overall survival (OS) of ~9–12 months[3,4]
- In the single-arm, phase 1b/2 CARTITUDE-1 study (NCT03548207; **Figure 1**), a single cilta-cel infusion induced early, deep, and durable responses in heavily treated patients with RRMM[1,2]
  - At median follow-up of 27.7 months, median duration of response (DOR), progression-free survival (PFS), and OS were not reached[2]
  - 27-month rates of PFS and OS were 54.9% and 70.4%, respectively[2]
- Cilta-cel was approved for the treatment of adult patients with RRMM after ≥4 (in the United States) or ≥3 (in Europe) prior lines of therapy (LOT), including an immunomodulatory drug (IMiD), a proteasome inhibitor (PI), and an anti-CD38 monoclonal antibody (mAb)[5,6]
- Here, we report study closeout results from CARTITUDE-1 at a median follow-up of 33.4 months

METHODS

Primary endpoints

- Phase 1b: Safety and dose
- Phase 2: Overall response rate (ORR)

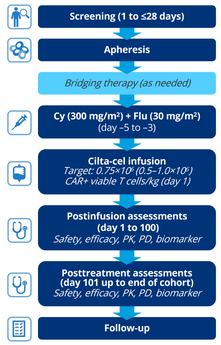
Secondary endpoints

- PFS
- OS
- Minimal residual disease (MRD) negativity at 10^{-5}

Key eligibility criteria

- Progressive multiple myeloma per International Myeloma Working Group criteria
- Eastern Cooperative Oncology Group performance status 0 or 1
- Measurable disease
- ≥3 prior LOT or double-refractory to a PI and IMiD
- Prior PI, IMiD, and anti-CD38 mAb exposure

FIGURE 1: CARTITUDE-1 study design



Cy, cyclophosphamide; Flu, fludarabine; PD, pharmacodynamics; PK, pharmacokinetics.

MULTIPLE MYELOMA

RESULTS

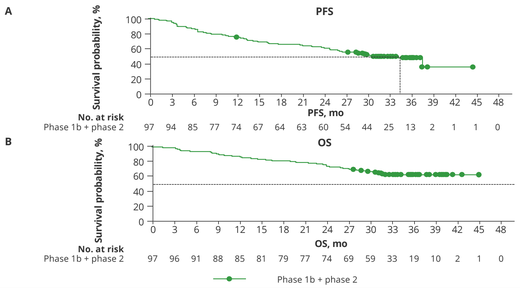
Study population

- As of October 14, 2022, 97 patients were treated with cilta-cel, with a median follow-up of 33.4 months (range, 1.5–45.2)
- Patient demographics and baseline characteristics have been previously described[1,2]
  - 42% of patients were penta-drug refractory, 88% were triple-class refractory, and 99% were refractory to last LOT
  - Patients received a median of 6 (range, 3–18) prior LOT

Efficacy

- The primary endpoint as assessed by independent review committee was previously reported:
  - ORR was 97.9% (95% CI, 92.7–99.7), and 82.5% (95% CI, 73.4–89.4) of patients achieved stringent complete response (sCR)[2]
- At study closeout:
  - Median DOR was 33.9 months (95% CI, 25.5–NE [not estimable])
  - Median PFS was 34.9 months (95% CI, 25.2–NE; **Figure 2A**)
  - Median OS was not reached (**Figure 2B**); an estimated 62.9% of patients were alive at 3-year follow-up

FIGURE 2: Time-to-event outcomes



- 62 patients had samples evaluable for MRD at any time, and 49 patients had samples evaluable for 12-month sustained MRD
  - Of these 49 evaluable patients, 26 had sustained MRD negativity for ≥12 months (**Table 1**)
    - Of the 26 patients, 20 had sustained MRD-negative complete response (CR) or better
- At 24 months after cilta-cel infusion, 18 patients remained MRD negative with ≥CR

TABLE 1: PFS by CR and sustained MRD negativity

Subgroups	mPFS (95% CI), mo	30-mo PFS rate	36-mo PFS rate
All patients	34.9 (25.2–NE)	54.2%	47.5%
≥CR[a]	38.2 (34.9–NE)	66.8%	59.8%
12-mo sustained MRD negativity[b]	NR (NE–NE)	74.9%	NE
12-mo sustained MRD-negative ≥CR[b]	NR (NE–NE)	78.5%	NE

[a]Patients had ≥CR at any time during the study, assessed by computerized algorithm. [b]Patients who were MRD evaluable had a baseline clone identified, sufficient follow-up for assessment, and ≥2 MRD-negative assessments 12 months apart, with no MRD-positive samples in that interval. mPFS, median progression-free survival; NR, not reached.

Safety

- No new neurotoxicity events were reported since the 27.7-month follow-up[2]
- A total of 26 second primary malignancies (SPMs) were reported in 20 patients
  - 4 new patients developed SPMs since 27.7-month median follow-up, with 6 new cases, including basal cell carcinoma (n=2) and 1 case each of myelodysplastic syndrome, B-cell lymphoma, melanoma, and prostate cancer
- A total of 35 deaths occurred (**Table 2**)
  - 5 new deaths unrelated to cilta-cel were reported since the 27.7-month median follow-up, including progressive disease (n=3), pneumonia (n=1), and sepsis (n=1)

TABLE 2: Study deaths

	Patients (N=97)	Time of death after cilta-cel infusion, days
Total deaths during the study	35	45–980
Due to progressive disease	17	253–980
AEs unrelated to treatment	**12**	
Pneumonia	2	109; 887
AML[a]	3	418; 582; 718
Ascites[b]	1	445
MDS	1	803
Respiratory failure	3	733; 793; 829
Septic shock and/or sepsis	2	917; 945
AEs related to treatment	**6**	
Septic shock and/or sepsis	2	45; 162
CRS/HLH	1	99
Lung abscess	1	119
Respiratory failure	1	121
Neurotoxicity	1	247

[a]One patient with AML also had MDS and a cytogenetic profile consistent with MDS (del(20q) [present before cilta-cel infusion], loss of 5q); another patient who died from AML had both prostate cancer and squamous cell carcinoma of the scalp. [b]Patient died from ascites (unrelated to cilta-cel as assessed by the investigator) due to noncirrhotic portal fibrosis and nonalcoholic steatosis that was present for many years preceding the study. AE, adverse event; AML, acute myelogenous leukemia; CRS, cytokine release syndrome; HLH, hemophagocytic lymphohistiocytosis; MDS, myelodysplastic syndrome.

KEY TAKEAWAY

At CARTITUDE-1 study closeout (~3-year follow-up), a single infusion of cilta-cel provided a median PFS of 34.9 months; treatment benefit of this magnitude has not been reported with any other therapy in this setting, including other BCMA-targeting CAR-T cell therapies

CONCLUSIONS

- An estimated 62.9% of patients were alive at 3-year follow-up, and there were no new neurotoxicity events
- Achieving CR and/or sustained MRD negativity was associated with prolonged PFS
- Patients continue to be followed for safety and survival in the 15-year CARTINUE long-term study (NCT05201781; MMY4002)[7]

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.

Previous presentation information: This poster has been previously presented at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting; June 2-6, 2023; Chicago, IL, US & Virtual.

DISCLOSURES

YL has served in a consulting or advisory role for Bluebird Bio, BMS, Celgene, Gamida Cells, Janssen, Juno, Kite/a Gilead Company, Legend Biotech USA Inc., Novartis, Pfizer, Sorrento Therapeutics, and Vineti; and has received research funding from Bluebird Bio Pharmaceuticals, BMS, Boston Scientific, Janssen, Kite/a Gilead Company, Merck, and Takeda. **TGM** has served in a consulting or advisory role for GSK and Legend Biotech USA Inc.; and has received research funding from Amgen, Janssen, and Sanofi. **SZU** has served in a consulting or advisory role for AbbVie, Amgen, BMS/Celgene, Celgene, Genentech, Gilead Sciences, GSK, Janssen, Karyopharm Therapeutics, Merck, and Takeda; and has received research funding from Amgen, Array BioPharma, BMS, Celgene, GSK, Merck, Pharmacyclics, Sanofi, Seattle Genetics, and SkylineDx. **JGB** has served in a consulting or advisory role for Bluebird Bio, BMS, CRISPR Therapeutics, Celgene, Janssen, Kite/a Gilead Company, Legend Biotech USA Inc., Roche, Secura Bio, and Takeda; and has received research funding from 2Seventy bio, AbbVie, Acetylon Pharmaceuticals, Amgen, Bluebird Bio, BMS, C4, CARsgen, Cartesian, Celgene, Celularity, CRISPR Therapeutics, EMD Serono, Fate, Genentech/Roche, GSK, Ichnos Sciences, Incyte, Janssen, Karyopharm Therapeutics, Lilly, Novartis, Poseida Therapeutics, Sanofi, Takeda, and Teva. **AJ** has served in a consulting or advisory role for AbbVie, Amgen, BMS, Celgene, Gracell, GSK, Janssen, Karyopharm Therapeutics, and Sanofi; and has received honoraria from AbbVie, Amgen, BMS, Celgene, Gracell, GSK, Janssen, Karyopharm Therapeutics, and Sanofi. **MEA** has stock and other ownership interests in GenCART, Inc. **ADC** has served in a consulting or advisory role for AbbVie, Arcellx, BMS, Celgene, Genentech/Roche, GSK, Ichnos Sciences, Janssen, Oncopeptides, and Pfizer; has received research funding from Genentech, GSK, Janssen, and Novartis; and has patents, royalties, or other intellectual property in Novartis. **AD** has served in a consulting or advisory role for Adicet Bio, Agios, Janssen, Juno/Celgene, Kite/a Gilead Company, and Novartis. **MH** has served in a consulting or advisory role and received travel, accommodations, and expenses from Millennium; and has received research funding from BMS and the Judy and Bernard Briskin Center for Multiple Myeloma Research. **AML** has served in a consulting or advisory role for Pfizer and Trillium Therapeutics; has patents, royalties, or other intellectual property in Serametrix, Inc.; received honoraria from Ikeis Therapeutics, Janssen, Legend Biotech USA Inc., Pfizer, Sanofi, and Trillium Therapeutics; and received research funding from BMS, Genentech, Janssen, Pfizer, Sanofi, and Trillium Therapeutics. **NCH** has served in a consulting or advisory role for AbbVie, Adaptive Biotechnologies, Amgen, BeiGene, BMS, Celgene, Janssen, Karyopharm Therapeutics, Novartis, OncoPep, Raqia, Sebia, and Takeda; has patents, royalties, or other intellectual property in OncoPep; and has stock or other ownership interests in C4, OncoPep, and Raqia Therapeutics. **EO** has served in a consulting or advisory role for BMS, Janssen, and Takeda. **CCJ** has served in a consulting or advisory role for Memorial Sloan Kettering Cancer Center; and is currently employed by Janssen. **T-MY** has stock or other ownership and is currently employed by Janssen. **AB** has stock or other ownership and is currently employed by Janssen. **EZ** has stock or other ownership, patents, royalties, or other ownership interests in Janssen; has received travel, accommodations, or expenses from Janssen; and is currently employed by Janssen. **DM** has served in a consulting or advisory role for Celgene, Foundation Medicine, GSK, Janssen, Legend Biotech USA Inc., and Takeda; has a family member receiving stock or other ownership interests from Roivant; and is currently employed by Janssen. **CdC** is currently employed by Legend Biotech USA Inc. **LP** is the Vice President of Clinical Development at Legend Biotech USA Inc.; has stock and other ownership interests in Legend Biotech USA Inc.; is currently employed by Legend Biotech USA Inc.; and has a family member with stock or ownership in Gilead Sciences. **SJ** has served in a consulting or advisory role for BMS, Janssen, Karyopharm Therapeutics, Legend Biotech USA Inc., Regeneron, Sanofi, and Takeda; and has received travel, accommodations, and expenses from BMS and Janssen.

REFERENCES:

1. Berdeja JG, et al. *Lancet.* 2021;398:314-24. **2.** Martin T, et al. *J Clin Oncol.* 2023;41:1265-74. **3.** Mateos M-V, et al. *Leukemia.* 2022;36:1371-76. **4.** Gandhi UH, et al. *Leukemia.* 2019;33:2266-75. **5.** CARVYKTI (ciltacabtagene autoleucel). Package insert. Janssen Biotech, Inc.; 2023. **6.** CARVYKTI® (ciltacabtagene autoleucel). European Medicines Agency. Orphan maintenance assessment report. June 7, 2022. Accessed March 23, 2023. https://www.ema.europa.eu/en/documents/orphan-maintenance-report/carvykti-orphan-maintenance-assessment-report-initial-authorisation_en.pdf. **7.** ClinicalTrials.gov. (NCT05201781).

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