PA-59

Long-Term (≥5-Year) Remission and Survival With Ciltacabtagene Autoleucel in Relapsed/Refractory Multiple Myeloma With 1–3 Prior Lines of Therapy: CARTITUDE-2 Cohort A

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Key Takeaway

Long-term phase 2 data suggest that earlier use of cilta-cel in patients with 1–3 prior LOT may be associated with a higher likelihood of durable 5-year remissions versus later-line use

- One in 2 patients in earlier lines
- One in 3 patients in later lines

Conclusions

Ten of 20 patients (50%) in CARTITUDE-2 cohort A treated with a single cilta-cel infusion remained alive and progression-free at ≥5 years without further anti-myeloma treatment. Median PFS was 60.5 months, and 5-year OS rate was 69.2%

No new cases of neurotoxicity were reported in long-term follow-up

Patients with durable 5-year remissions showed a trend towards lower baseline tumor burden

Patients with durable 5-year remissions had higher CD4⁺ naive T-cell levels at apheresis and higher levels of CAR⁺ CD4⁺ central memory T cells at peak expansion

Only cilta-cel has demonstrated evidence of durable 5-year treatment-free remissions in RRMM, now with 50% of patients in remission in a CARTITUDE-4–like population

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Poster

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Acknowledgments

The authors, Johnson & Johnson, and Legend Biotech USA Inc. thank the patients who participated in this study, the staff members at the study sites, the data and safety monitoring committee, and the staff members involved in data collection and analyses. The authors thank Vicki Plaks and Katerine Li for their assistance with data analyses and critical review of the presentation. This study was funded by Johnson & Johnson and Legend Biotech USA Inc. Medical writing support was provided by Priyanka D. Pinky, PhD, CMPP, Francesca Balordi, PhD, CMPP, and Alanna Kennedy, PhD, CMPP, of The Lockwood Group (Stamford, CT, USA), in accordance with Good Publication Practice (GPP 2022) guidelines, and funded by Johnson & Johnson and Legend Biotech USA Inc.

Disclosures

ADC has the following disclosures: **Consulting or Advisory Role:** AbbVie, Arcellx, AstraZeneca, Bristol Myers Squibb, Caribou Biosciences, GlaxoSmithKline, Ichnos Sciences, ITeos Therapeutics, Janssen Oncology, Kite Pharma (a Gilead company), Moderna, Novartis, Pfizer, Inc., Prothena, Regeneron, Roche/Genentech, and Sanofi; **Research Funding:** Genentech/Roche (Inst), GlaxoSmithKline (Inst), Janssen Oncology (Inst), and Novartis (Inst); **Patents, Royalties, Other Intellectual Property:** Patents related to CAR T cells and biomarkers of cytokine release syndrome; **Travel, Accommodations, Expenses:** AbbVie, Bristol Myers Squibb, Ichnos Sciences, and Janssen Oncology

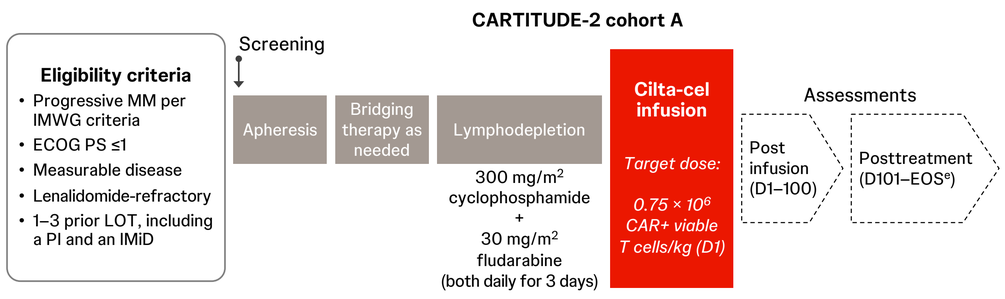
Introduction

- In CARTITUDE-1, a single infusion of ciltacabtagene autoleucel (cilta-cel) yielded deep and durable responses in heavily pretreated patients with relapsed/refractory multiple myeloma (RRMM)[1]
  - 33% of patients remained alive and progression-free at ≥5 years
  - Median overall survival (OS) was 60.7 months
- CARTITUDE-2 (NCT04133636) is a phase 2 multicohort study evaluating cilta-cel in patients with multiple myeloma in various clinical settings[2-4]
  - Cohort A (initial subgroup) includes patients with 1–3 prior lines of therapy (LOT) who were exposed to a proteasome inhibitor (PI) and were lenalidomide-refractory
  - Data from a prior analysis with a median follow-up of approximately 30 months were published previously[2]

Here, we report updated efficacy and safety results from CARTITUDE-2 cohort A after a median follow-up of 60.7 months, with all patients ≥5 years from cilta-cel infusion

Methods

Figure 1: Cohort A includes patients with 1–3 prior LOT exposed to PI and lenalidomide-refractory



- **Primary endpoint:** Rate of MRD negativity[a] (10^{-5} threshold) by NGS/NGF by central laboratory
- **Secondary endpoints:** ORR,[a] DOR, time to response, safety[b]
- **Exploratory endpoints:** PFS[a,c] and OS[d]

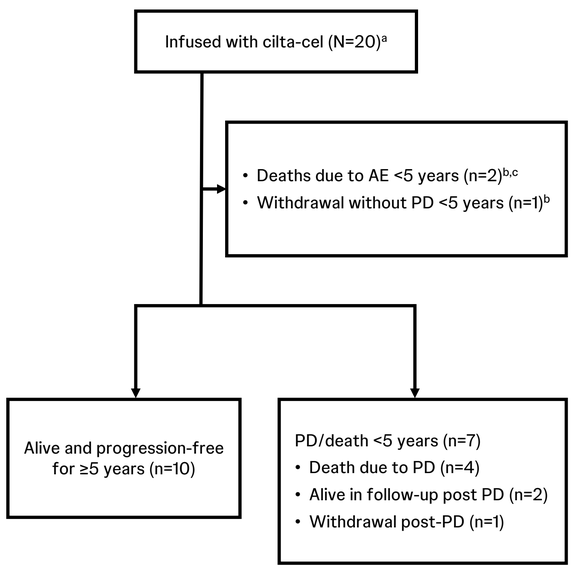
[a]According to IMWG criteria. [b]AEs were coded using MedDRA, version 24.0, and graded according to NCI-CTCAE, version 5.0, with the exception of CRS and CAR T-cell–related neurotoxicity (eg, ICANS), which were graded according to the ASTCT consensus grading system.[5] [c]Time from cilta-cel infusion to disease progression/death. [d]Time from cilta-cel infusion to death. [e]EOS was defined as 2 years after the last patient in cohort A who received cilta-cel infusion.
AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; D, study day; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EOS, end of study; ICANS, immune effector cell–associated neurotoxicity syndrome; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; LOT, line of therapy; MRD, minimal residual disease; MM, multiple myeloma; NCI, National Cancer Institute; NGF, next-generation flow; NGS, next-generation sequencing; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; SOC, standard of care.

- After cohort completion, patients were asked to enroll into CARTinue (NCT05201781), a 15-year post-infusion follow-up study
  - 14 of the 20 eligible patients enrolled into CARTinue (5 died and 1 with PD declined participation in CARTinue)

Results

Patients

Figure 2: With a median follow-up of 60.7 months (range, 3.3–63.1), 10 of 20 patients (50%) remained alive and progression-free without further anti-myeloma treatment ≥5 years after cilta-cel infusion



[a]Eighteen of 20 patients (90.0%) who received cilta-cel infusion also received bridging therapy to maintain disease stability between apheresis and initiation of the conditioning regimen. [b]These patients are excluded from correlative analyses. [c]Death without PD (sepsis and COVID-19 lung infection, n=1 each).
AE, adverse event; cilta-cel, ciltacabtagene autoleucel; PD, progressive disease.

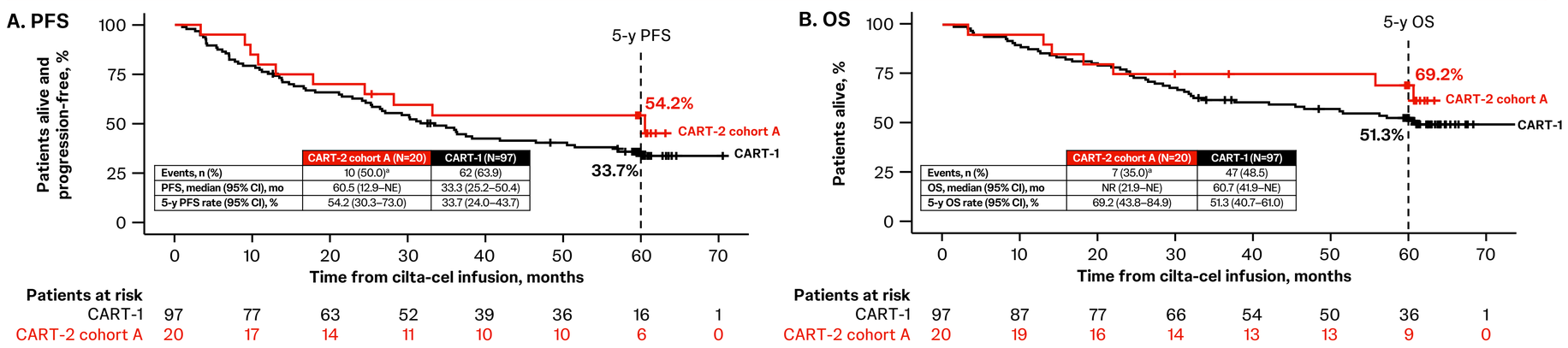
Table 1: Baseline characteristics by durable response group:
- **A trend towards lower baseline tumor burden in durable responders (as measured by soluble BCMA and bone marrow plasma cell %) versus those who died or progressed by year 5**
- **60% of durable responders had a decrease in tumor burden[a] from screening to cilta-cel infusion (vs 42.9% of patients who died or progressed by year 5)**
- **Five of 7 (71.4%) durable responders with available cytogenetic risk status at baseline had ≥1 high-risk cytogenetic feature; 4 of 7 had ≥2 high -risk cytogenetic features**
- **Five of 10 (50%) durable responders were refractory to daratumumab**
- **Median time from start of last LOT to progression on that line was numerically higher in patients with durable responses versus those who died or progressed by year 5 (12.8 vs 5.7 months)**

Characteristic	Alive and progression-free for ≥5 years (n=10)	PD/death due to PD <5 years (n=7)
Age, years, median (range)	60.5 (47–68)	57.0 (38–61)
Male, n (%)	6 (60.0)	5 (71.4)
High-risk cytogenetics, n/N (%)		
Any of the 5 abnormal markers[b]	5/7 (71.4)	7/7 (100.0)
≥2 of the 5 abnormal markers[b]	4/7 (57.1)	3/7 (42.9)
Excluding gain/amp(1q)	5/7 (71.4)	3/7 (42.9)
Standard risk cytogenetics, n/N (%)	2/7 (28.6)	0
% bone marrow plasma cells, median (range)[c]	20.0 (1.0–95.0)	40.0 (4.7–95.0)
% bone marrow plasma cells, n (%)[c]		
≤30%	9 (90.0)	3 (42.9)
>30% to <60%	0	2 (28.6)
≥60%	1 (10.0)	2 (28.6)
Soluble BCMA, µg/L, median (range)[d]	14.1 (4.3–982.3)	68.2 (7.4–132.6)
Any decrease in tumor burden from screening to cilta-cel infusion, n (%)[a]	6 (60.0)	3 (42.9)
Presence of soft tissue plasmacytomas, n (%)[e]	2 (20.0)	1 (14.3)
Previous LOT, median (range)	2 (1–3)	3 (1–3)
Prior ASCT, n (%)	9 (90.0)	5 (71.4)
Triple-class exposure, n (%)[f]	5 (50.0)	6 (85.7)
Triple-class refractory, n (%)[f]	4 (40.0)	3 (42.9)
Daratumumab exposed, n (%)	5 (50.0)	6 (85.7)
Daratumumab refractory, n (%)	5 (50.0)	5 (71.4)
Time from start of last LOT to progression on that line, months, median (range)	12.8 (1.5–43.2)	5.7 (1.0–41.7)

[a]Tumor burden between screening and cilta-cel infusion was measured based on the patient's baseline measurable disease: serum M-protein, urine M-protein, or difference between involved and uninvolved FLC. [b]The 5 abnormal markers are: del(17p), t(4;14), t(14;16), t(14;20), gain/amp(1q). [c]Maximum value from bone marrow biopsy and bone marrow aspirate was selected if both results were available. [d]Last non-missing record on or before cilta-cel infusion. [e]Includes extramedullary soft tissue plasmacytoma and bone-related soft tissue plasmacytoma. [f]Triple-class was defined as ≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 antibody.
amp, amplification; ASCT, autologous stem cell transplantation; BCMA, B-cell maturation antigen; cilta-cel, ciltacabtagene autoleucel; FLC, free light chain; IMiD, immunomodulatory drug; LOT, line of therapy; PD, progressive disease; PI, proteasome inhibitor.

Efficacy

Figure 3: Earlier use of cilta-cel was associated with numerically higher PFS and OS than observed in CARTITUDE-1 which enrolled patients with ≥3 prior LOT



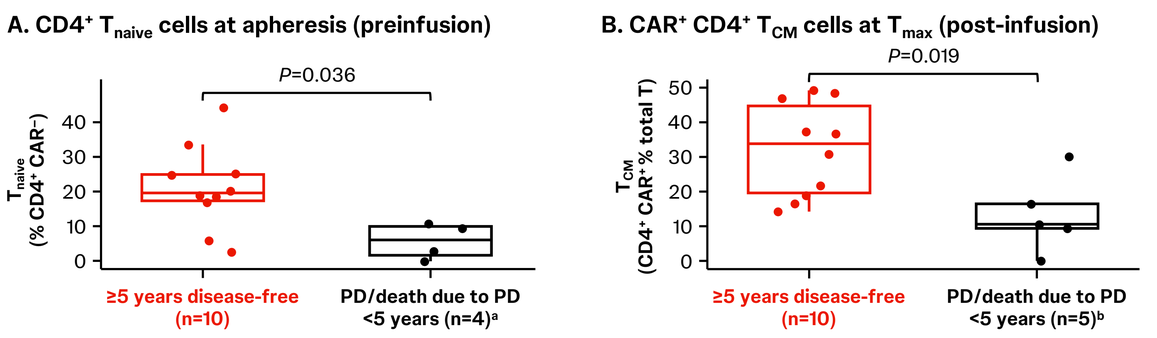
[a]In C-2 cohort A, 1 PFS/OS event after 5 years was a death due to unrelated breast cancer without progression of myeloma.
CART-1, CARTITUDE-1; CART-2, CARTITUDE-2; cilta-cel, ciltacabtagene autoleucel; LOT, line of therapy; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival.

- **95% (19/20) of patients achieved CR/stringent CR as their best response. One patient had minimal response and died due to COVID-19 pneumonia**
- **Three patients among those alive and progression-free at ≥5 years underwent assessment by bone marrow at ≥5 years (not required per protocol) and all were MRD-negative (at the 10^{-6} threshold)**

CR, complete response; MRD, minimal residual disease.

Biomarker correlates of durable response

Figure 4: Patients alive and progression-free at ≥5 years had significantly higher CD4⁺ naive T-cell levels at apheresis and higher levels of CAR⁺ CD4⁺ central memory T cells at peak expansion versus those post-PD <5 years. These two covariates were associated with prolonged PFS in patients in CARTITUDE-4 and long-term remission ≥5 years after infusion in CARTITUDE-1[1,6]



[a]Biomarker data for 3 patients in the PD/death due to PD <5 years group were not available. [b]Biomarker data for 2 patients in the PD/death due to PD <5 years group were not available. T_{naive} and T_{CM} cells were defined by CD27, CD45RO, and CD95 antibodies for immunophenotyping.
CAR, chimeric antigen receptor; PD, progressive disease; T_{CM}, central memory T cells; T_{max}, sampling time (days post-infusion) to reach maximum concentration (C_{max}).

Safety

Table 2: Safety update since the last CARTITUDE-2 report (N=20)

Events, n (%)	New since last report (at 30-month follow-up)
Second primary malignancy (not related to cilta-cel)[a]	5 (25.0)
Acute myeloid leukemia	1 (5.0)
Breast cancer	1 (5.0)
Prostate cancer	1 (5.0)
Basal cell carcinoma	1 (5.0)
Malignant melanoma stage 0 (melanoma in situ)	1 (5.0)
Squamous cell carcinoma	1 (5.0)
CAR T-cell–related neurotoxicity	
Cranial nerve palsies	0
Parkinsonism	0
Overall mortality	2 (10.0)
Death due to AE	1 (5.0)[b]

[a]One patient had 2 second primary malignancies: basal cell carcinoma and malignant melanoma stage 0. [b]The patient who died due to breast cancer was alive and progression-free at 5 years.
AE, adverse event; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel.

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Multiple Myeloma

Presented by AD Cohen at the International Myeloma Society (IMS) Annual Meeting; September 23–26, 2026; Glasgow, Scotland