Long-Term (≥5 Year) Remission and Survival After Treatment With Ciltacabtagene Autoleucel in CARTITUDE-1 Patients With Relapsed/Refractory Multiple Myeloma

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CARTITUDE-1 Long-Term Remission: Key Takeaways

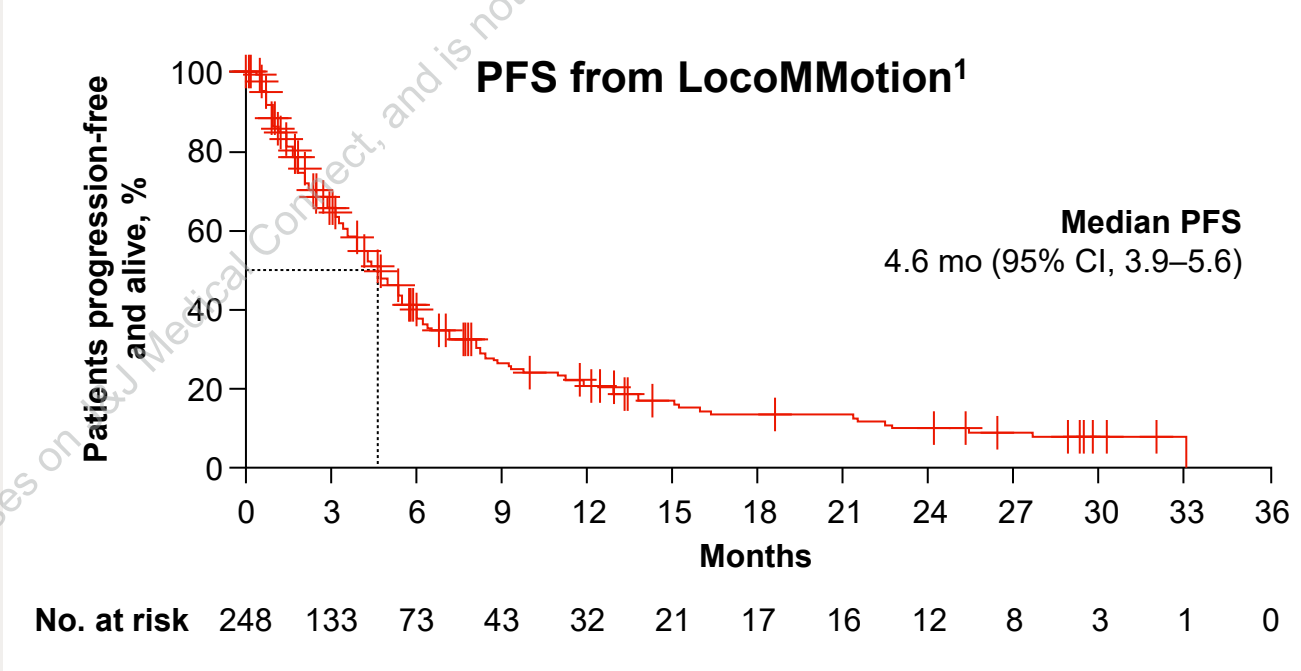
- One-third (33%) of the patients with heavily pretreated, mostly triple-class refractory MM in the pivotal CARTITUDE-1 study[a] remained progression-free for ≥5 years following a single cilta-cel infusion with no maintenance therapy
- Approximately half the patients were alive for ≥5 years
- Of the patients who were progression-free, serial MRD assessments were conducted on 12 patients at a single center
  - All were MRD-negative (at least 10^{-5} threshold) and PET/CT imaging-negative at ≥5 years after cilta-cel without additional therapy, suggesting potential cure

We report the first evidence of the curative potential of cilta-cel in relapsed/refractory MM

[a]Median 61.3 months follow-up.
cilta-cel, ciltacabtagene autoleucel; MM, multiple myeloma; MRD, minimal residual disease; PET/CT, positron emission tomography/computed tomography.

CARTITUDE-1 Long-Term Remission: Introduction

- Historically, expected **mPFS was <6 months** and **mOS was ~1 year** in heavily pretreated RRMM[1]
- In the CARTITUDE-1[a] study of cilta-cel (BCMA CAR-T) in triple-class exposed RRMM, where median time to progression on last prior LOT was ~4 months[2]:
  - Median PFS after cilta-cel was 34.9 months and mOS was not reached at 33.4-month median follow-up[3]
  - Sustained MRD negativity was associated with prolonged PFS[3]



We report the 5-year[b] follow-up from the pivotal CARTITUDE-1 study of cilta-cel in RRMM

[a]CARTITUDE-1 is a phase 1b/2 trial; NCT03548207. [b]Median 61.3 months.
BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; LOT, line of therapy; mOS, median overall survival; mPFS, median progression-free survival; MRD, minimal residual disease; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma.
1. Mateos MV, et al. *Leukemia* 2024;38:2554-60. 2. Berdeja JG, et al. *Lancet* 2021;398:314-24. 3. Lin Y, et al. *JCO* 2023;41:8009.

Study Design and Endpoints

Eligibility criteria

- Progressive MM per IMWG criteria
- ECOG PS ≤1
- Measurable disease
- ≥3 prior LOT or double refractory to a PI and an IMiD
- Prior PI, IMiD, and anti-CD38 mAb exposure

CARTITUDE-1

Screening

Apheresis → Bridging therapy (As needed) → Lymphodepletion → **Cilta-cel infusion** *Target dose: 0.75×10^6 CAR+ viable T cells/kg (day 1)* → Posttreatment follow-up

CARTinue

15-year postinfusion follow-up study

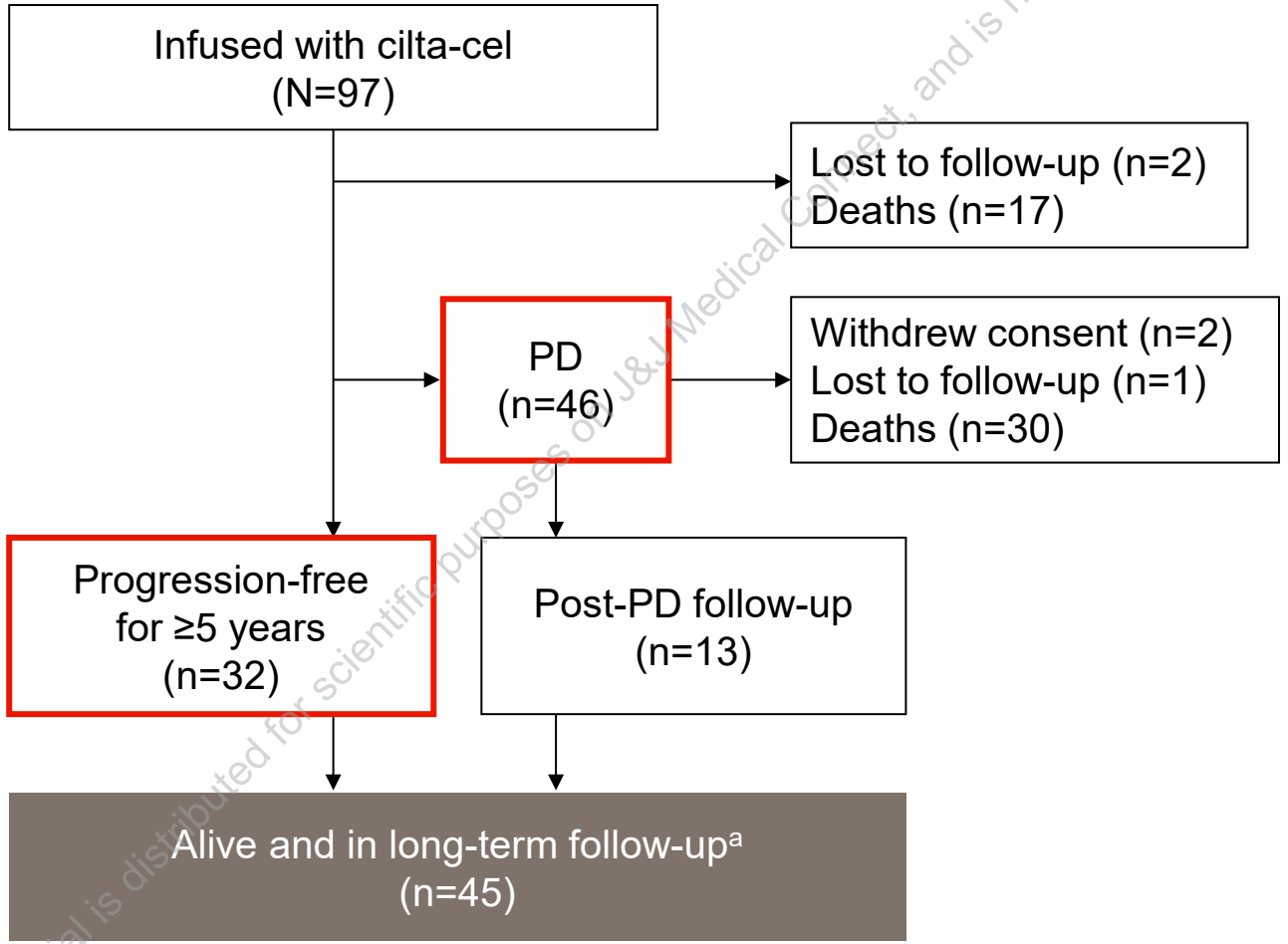
Patient evaluations per local standard of care (reported annually at minimum)

Analyses (N=97)

- Phase 1b (n=29) and phase 2 (n=68)
- Efficacy and safety
- Postinfusion assessments[a] (day 1–100)
- Posttreatment assessments[a] (day 101–end of cohort)
- Biomarker correlative analyses[b]

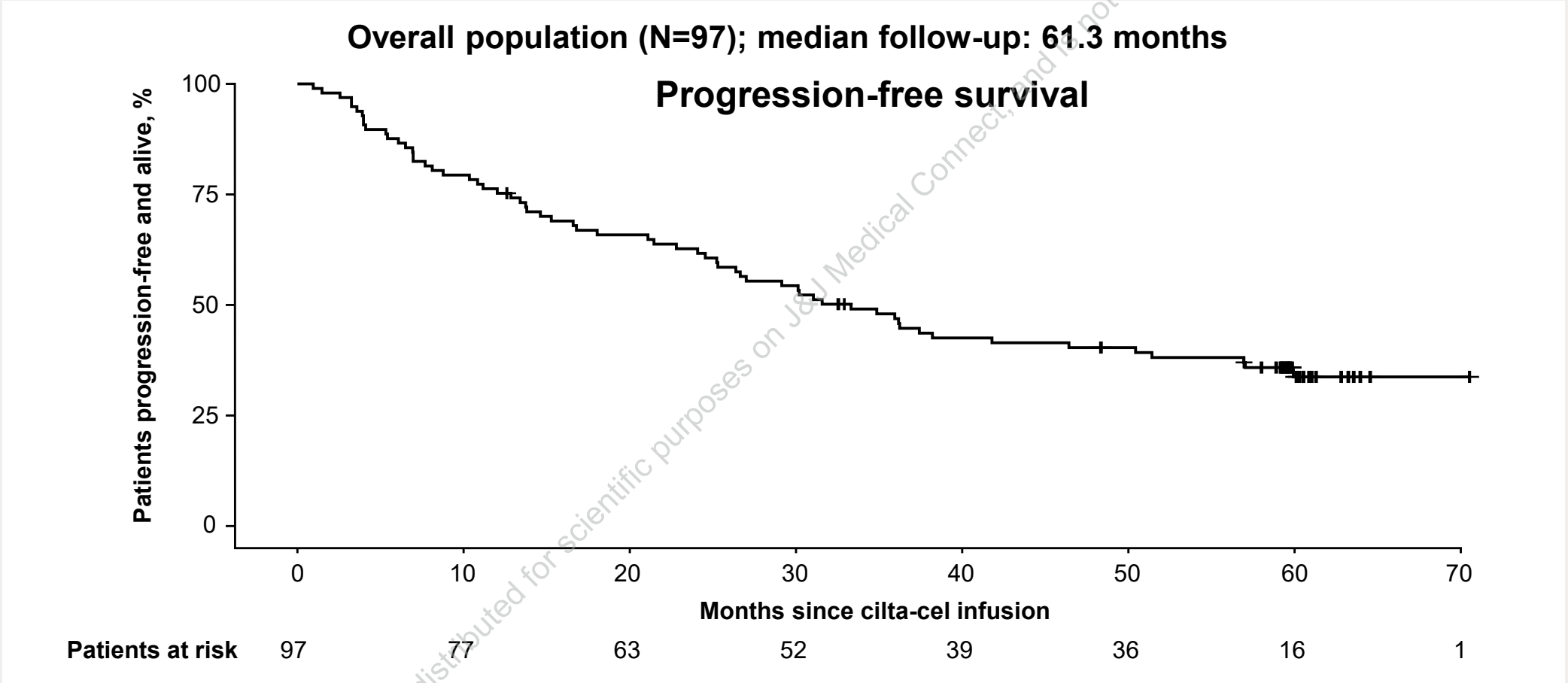
[a]Longitudinal preinfusion and postinfusion data on pharmacokinetics, pharmacodynamics, and disease assessments. [b]Analyses were performed utilizing preinfusion samples (collected at the time of apheresis, prior to conditioning, or on day 1 prior to infusion depending on the biomarker), drug product, and postinfusion samples. CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; LOT, line of therapy; mAb, monoclonal antibody; MM, multiple myeloma; MRD, minimal residual disease; PI, proteasome inhibitor.

CARTITUDE-1 Long-Term Remission: Patient Disposition



[a]At median 61.3-month follow-up.
cilta-cel, ciltacabtagene autoleucel; PD, progressive disease.

CARTITUDE-1 Long-Term Remission: One-Third of Patients Were Progression-Free for ≥5 Years

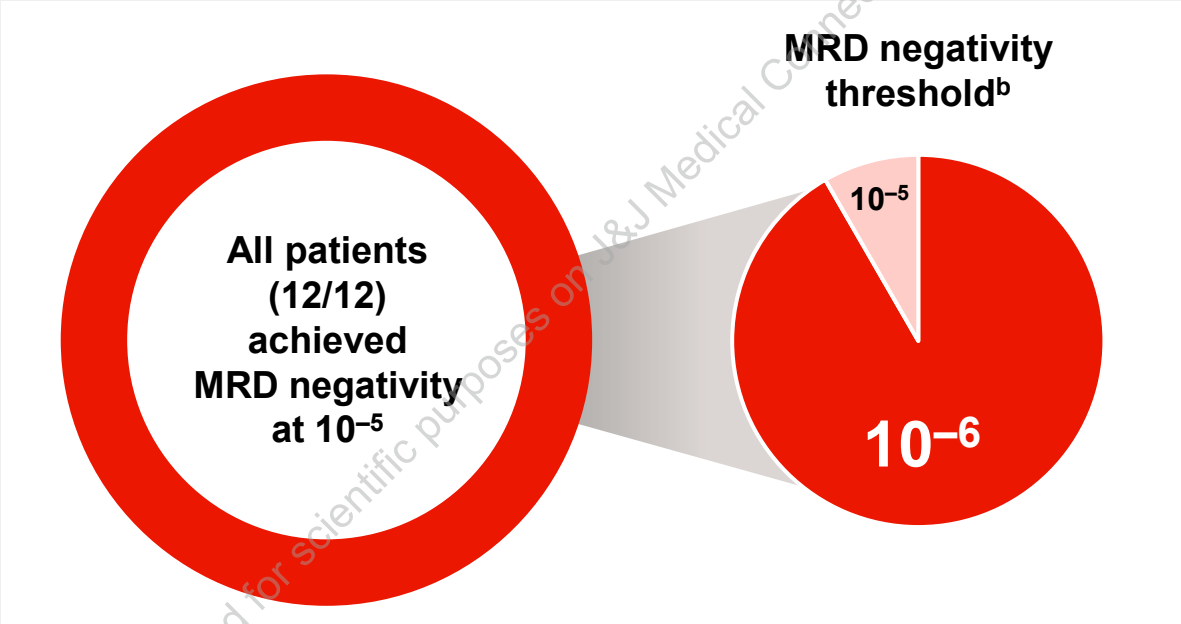


32 of 97 (33%) patients were treatment- and progression-free at ≥5 years

cilta-cel, ciltacabtagene autoleucel.

CARTITUDE-1 Long-Term Remission: Sustained MRD Negativity in All Long-Term Responders at a Single Center

- Of the patients who were progression-free, 12 patients in stringent complete response from a single center underwent serial MRD and PET/CT assessments[a]



All patients (12/12) were MRD-negative[b] and imaging-negative at year 5 or later following cilta-cel infusion

[a]Of the remaining 20 patients (from the 32 who were progression-free at ≥5 years), during the course of CARTITUDE-1, 12 patients were MRD-negative at 10^{-6}, 1 was MRD-positive, and the rest were unevaluable (5 had no clone identified, 1 failed QC, and 1 was indeterminate). [b]The 1 patient who was MRD-negative at 10^{-5} was determined by flow cytometry.
cilta-cel, ciltacabtagene autoleucel; MRD, minimal residual disease; PET/CT, positron emission tomography/computed tomography; QC, quality control.

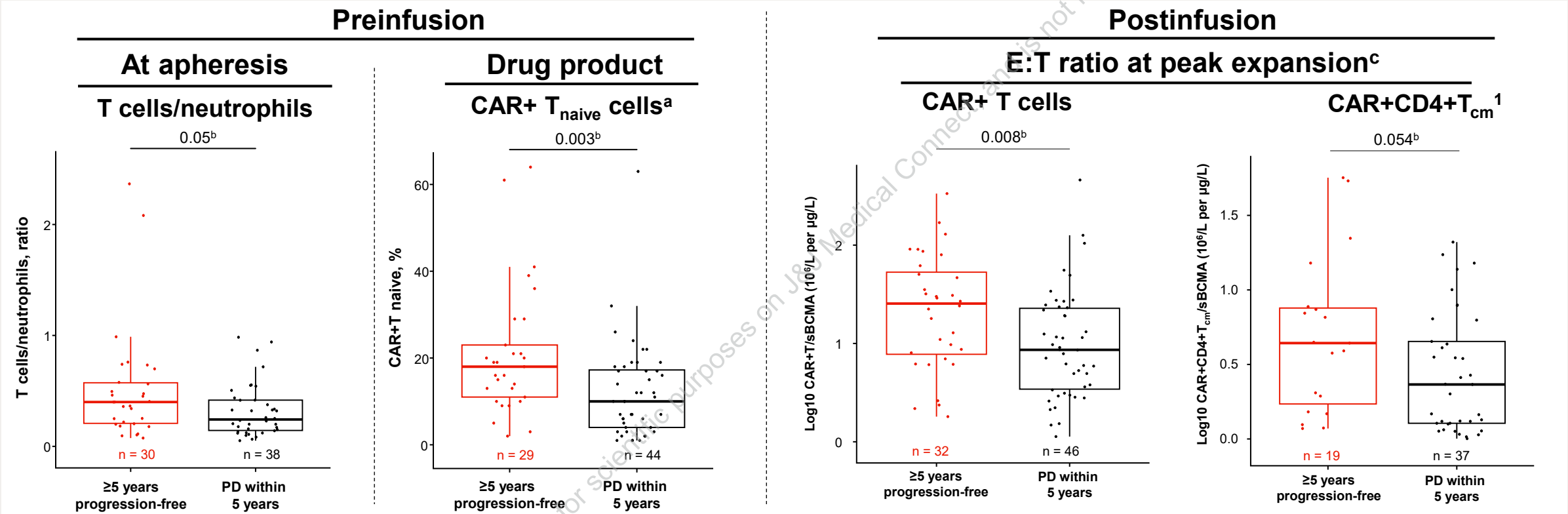
CARTITUDE-1 Long-Term Remission: Baseline Demographics and Disease Characteristics Were Generally Comparable Between Patients With or Without PD Within 5 Years (Post Hoc Analyses)

	≥5 years progression-free (n=32)	PD within 5 years (n=46)
Age, years, median (range)	60.0 (43–78)	61.5 (47–77)
High-risk cytogenetics,[a] n/N (%)	**7/30 (23.3)[b]**	**12/45 (26.7)**
Extramedullary plasmacytomas, n (%)	**4 (12.5)[c]**	**6 (13.0)**
Time to progression on last prior LOT, months, median (range)	3.98 (0.7–48.6)[d]	3.89 (0.7–21.5)[e]
Prior LOT, median (range)	6.5 (3–14)	5.0 (3–18)
Triple-class[f] refractory, n (%)	29 (90.6)	39 (84.8)
Penta-drug[g] refractory, n (%)	15 (46.9)	15 (32.6)
Bone marrow plasma cells, %, median (range)	**5.0 (0.8–80.0)**	**24.0 (0.0–95.0)**
Soluble BCMA, µg/L, median (range)	**36.0 (3.7–864.6)**	**58.5 (3.8–1342.9)**
High baseline tumor burden,[h] n (%)	2 (6.3)	8 (17.4)

Patients with high-risk cytogenetics and extramedullary plasmacytomas were equally likely to be progression-free. Of note, the percentage of patients with high tumor burden was numerically lower among patients who were progression-free

[a]Either del17p, t(14;16), or t(4;14). [b]4 patients had del17p, 2 had t(14;16), and the remaining 1 patient had a double hit of del17p and t(14;16). [c]Extramedullary disease denotes soft tissue plasmacytoma that was not contiguous with bone. [d]n=29. [e]n=42. [f]≥1 PI, ≥1 IMiD, and 1 anti-CD38 antibody. [g]≥2 PIs, ≥2 IMiDs, and 1 anti-CD38 antibody. [h]Low tumor burden defined as meeting all following parameters (as applicable): bone marrow % plasma cells <50%, serum M protein <3 g/dL, serum FLC <3000 mg/L. High tumor burden defined as meeting any of the following parameters: bone marrow % plasma cells ≥80%, serum M protein ≥5 g/dL, serum FLC ≥5000 mg/L. Intermediate tumor burden did not fit either criteria of high or low tumor burden. 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.

CARTITUDE-1 Long-Term Remission: Long-Term Disease Control Was Associated With Fitter Immune T Cells Before Infusion and Higher E:T Ratio After Infusion

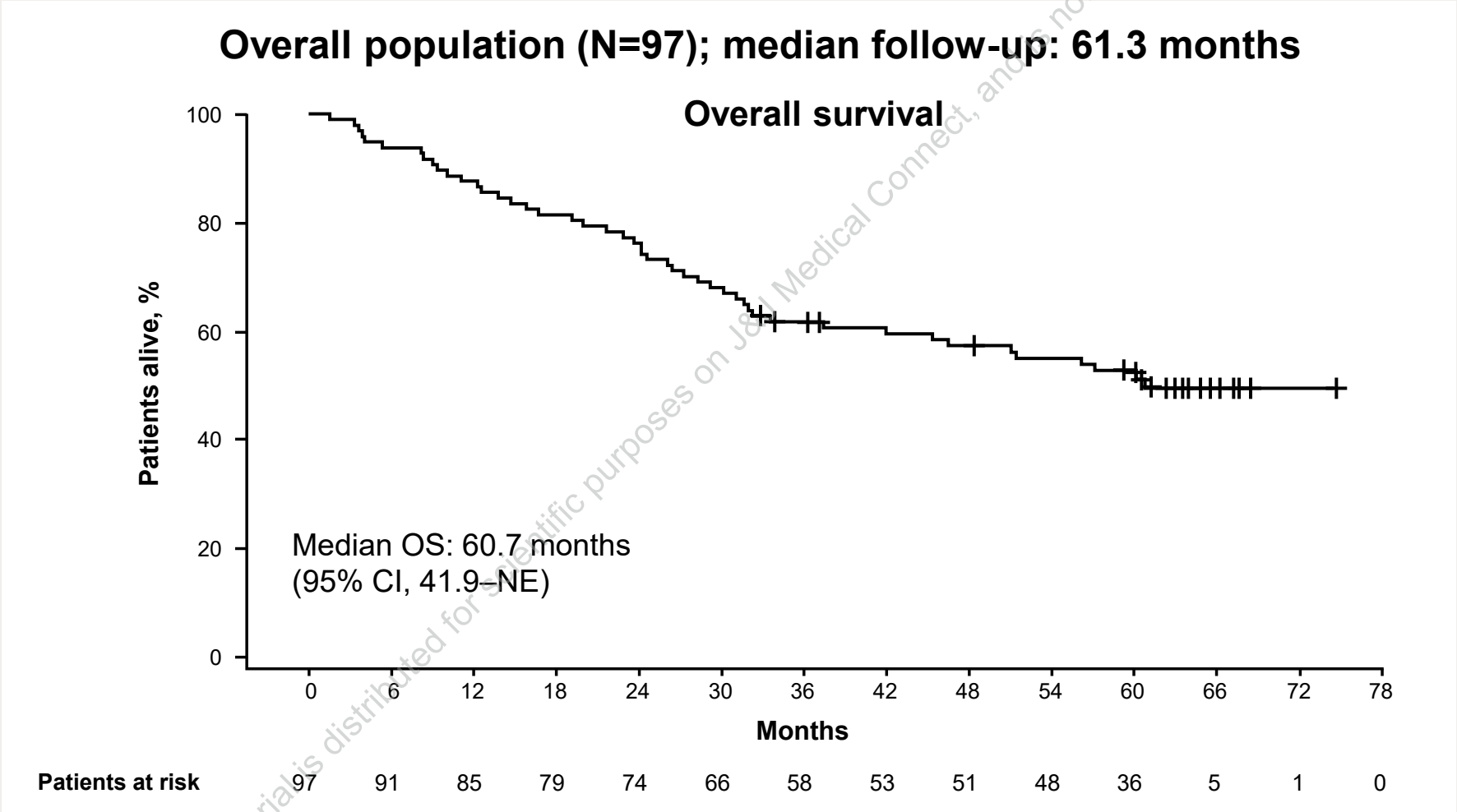


Long-term disease control was significantly associated with:

- Higher T cells over neutrophil ratio
- Fitter T_{naive} cells in the drug product
- Higher overall E:T ratio with either total CAR+ T cells or CAR+ CD4+ T cells with central memory phenotype at peak expansion

[a]CAR+ T_{naive} cells were defined as CD95-CD27+CD45RO-. [b]2-sided nominal *P* values unadjusted for multiplicity were provided for descriptive purposes. These analyses were exploratory in nature and utilized for hypothesis generation.
[c]E:T ratio was defined as maximal CAR-positive T-cell levels normalized by preinfusion serum sBCMA levels.
CAR, chimeric antigen receptor; E:T, effector to target; PD, progressive disease; sBCMA, soluble B-cell maturation antigen; T_{cm}, central memory T cell; T_{naive}, naive T cell.
1. Ledergor G, et al. *Blood Adv* 2024;8:3562-75.

CARTITUDE-1 Long-Term Remission: Median Overall Survival Was 5 Years



NE, not estimable; OS, overall survival.

CARTITUDE-1 Long-Term Remission: Safety Profile of Cilta-cel Remained Consistent in Patients in Long-Term Remission

In patients ≥5 years progression-free (n=32) with an additional ~28 months[a] median follow-up:

- No new cases of parkinsonism or cranial nerve palsy
- 2 additional cases each of
  - SPMs (both solid tumors)[b]
  - Neurologic events (not related to cilta-cel)
    - 1 case each of encephalopathy and taste disorder
- 4 new-onset grade 3 infections (not related to cilta-cel)

[a]Last median follow-up was 33.4 months. At 33.4-month median follow-up, no new neurotoxic events were reported since the 27.7-month median follow-up; a total of 26 SPMs were reported in 20 patients of which there were 6 new cases in 4 patients at 33.4-month median follow-up. [b]1 case each of lung adenocarcinoma and anal squamous carcinoma. cilta-cel, ciltacabtagene autoleucel; SPM, second primary malignancy.

CARTITUDE-1 Long-Term Remission: Conclusions

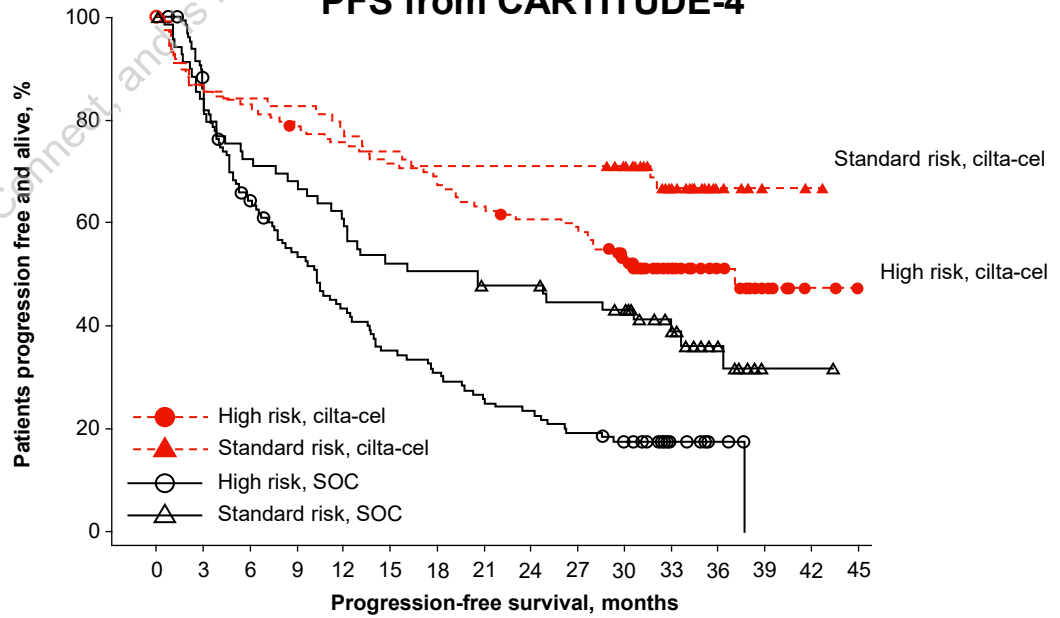
- One-third (33%, n=32) of the patients with a historical mPFS of <6 months remain progression-free for ≥5 years following a single cilta-cel infusion with no maintenance or subsequent therapy
  - Of the progression-free patients, 12 from a single center with serial MRD assessments were all MRD- and imaging-negative at year 5 or longer, suggesting potential cure
- Long-term remission was not limited to standard-risk disease
  - Patients with high-risk cytogenetics [ie, del17p, t(14;16), or t(4;14)] and those with extramedullary plasmacytomas were equally likely to be progression-free
- Patients in long-term remission had more immune-fit drug products and higher E:T ratio at peak expansion
- Median OS of 5 years sets a new benchmark in this population

Long-term follow-up from CARTITUDE-1, with one-third of patients remaining treatment- and progression-free for at least 5 years after a single infusion, shows the curative potential of cilta-cel in RRMM

cilta-cel, ciltacabtagene autoleucel; E:T, effector to target; mPFS, median progression-free survival; MRD, minimal residual disease; OS, overall survival; RRMM, relapsed/refractory multiple myeloma.

CARTITUDE-1 Long-Term Remission: Cilta-cel Future Directions

- Earlier use of cilta-cel may further extend long-term remissions due to:
  - Fitter CAR-T cell profiles
  - More effective bridging therapies prior to manufacturing to improve E:T ratios
- CARTITUDE-4 PFS curve in patients with standard-risk disease after 1–3 prior LOT suggests a plateau
- CARTITUDE-5[1] and CARTITUDE-6[2] are evaluating the impact of cilta-cel in newly diagnosed MM vs standard of care with the potential to demonstrate cure and replace transplant (CARTITUDE-6)



Patients at risk

High risk, SOC	132	111	79	65	52	42	37	31	28	23	20	7	3	0	0	0
High risk, cilta-cel	123	106	102	96	92	87	84	76	73	70	55	31	14	7	2	0
Standard risk, SOC	70	58	50	47	41	36	35	32	32	29	27	18	9	1	1	0
Standard risk, cilta-cel	69	59	58	57	53	51	49	49	49	49	46	27	9	2	1	0

[Poster 7539: Sidana S, et al. Cilta-cel vs SOC in Patients With RRMM: CARTITUDE-4 Survival Subgroup Analyses. June 1, 2025; 9AM–12PM CDT]

CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; E:T, effector-to-target; LOT, line of therapy, MM, multiple myeloma; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma; SOC, standard of care.
1. https://clinicaltrials.gov/study/NCT04923893. Accessed April 8, 2025. 2. https://clinicaltrials.gov/study/NCT05257083. Accessed April 8, 2025.

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Clinical Trial Updates

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ABSTRACT

CARTITUDE-1 evaluated ciltacabtagene autoleucel (cilta-cel) in patients with heavily pretreated relapsed/refractory multiple myeloma (RRMM). We describe overall survival (OS), ≥5-year progression-free outcomes, associated biomarkers, and safety, with a median study follow-up of 61.3 months. For the 97 treated patients, median OS was 60.7 months (95% CI, 41.9 to not estimable). One third (32/97) of patients remain alive and progression-free for ≥5 years after a single cilta-cel infusion, without maintenance treatment. Twelve of these patients treated at a single center underwent serial minimal residual disease (MRD) and positron emission tomography–computed tomography assessments, and all (100%) were MRD-negative (at least 10^{-5} threshold) and imaging-negative at year 5 or later after cilta-cel. Baseline characteristics, including the presence of high-risk cytogenetics and extramedullary disease, were generally comparable for the 32 patients who were progression-free for ≥5 years versus patients who had progressive disease by year 5. A trend of lower baseline tumor burden, higher fraction of naïve T-cells in the cilta-cel drug product, higher T cell–to–neutrophil ratio, higher hemoglobin and platelets at baseline, and higher effector-to-target ratio were associated with ≥5-year progression-free status. The safety profile of cilta-cel remained consistent with previous reports. To our knowledge, our data provide the first evidence that cilta-cel is potentially curative in patients with RRMM.

ACCOMPANYING CONTENT

Data Sharing Statement
Data Supplement
Protocol

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View Online Article

INTRODUCTION

For patients with heavily pretreated relapsed/refractory multiple myeloma (RRMM), previous studies report a median progression-free survival (PFS) of <6 months and median overall survival (mOS) of approximately 1 year.[1,2] Ciltacabtagene autoleucel (cilta-cel), a B-cell maturation antigen (BCMA)–directed CAR-T cell therapy, led to deep and durable responses in heavily pretreated patients with RRMM in the phase Ib/II CARTITUDE-1[3,4] trial, and significantly prolonged PFS and overall survival (OS) in patients with 1-3 previous lines in the phase III CARTITUDE-4[5,6] trial.

The primary end points of CARTITUDE-1 were safety (phase Ib) and efficacy (overall response rate; phase II). Study closeout results (median follow-up, 33.4 months) were previously reported.[7] Briefly, median PFS was 34.9 months, and mOS was not reached.[7] On the basis of CARTITUDE-1, cilta-cel was initially approved in the United States for patients with RRMM after ≥4 previous lines of therapy (LOT),[8] and subsequently expanded to relapsed, lenalidomide-refractory MM with ≥1 previous LOT on the basis of CARTITUDE-4.[5,7,9]

To gain additional insight into those patients who had long-term clinical benefit ≥5 years after a single cilta-cel infusion, we conducted a post hoc analysis. We report OS, ≥5-year progression-free outcomes, associated biomarkers, and safety from CARTITUDE-1, with 61.3-month median follow-up.

METHODS

Study Design

CARTITUDE-1 (ClinicalTrials.gov identifier: NCT03548207) was a phase Ib/II, open-label, multicenter study of cilta-cel in patients with RRMM. The study design was previously reported.[3,4] Enrolled patients had RRMM, ≥3 previous LOT, and were triple-class exposed (Data Supplement, online only). After CARTITUDE-1 completion, patients were offered enrollment into CARTinue (ClinicalTrials.gov identifier:

ascopubs.org