# 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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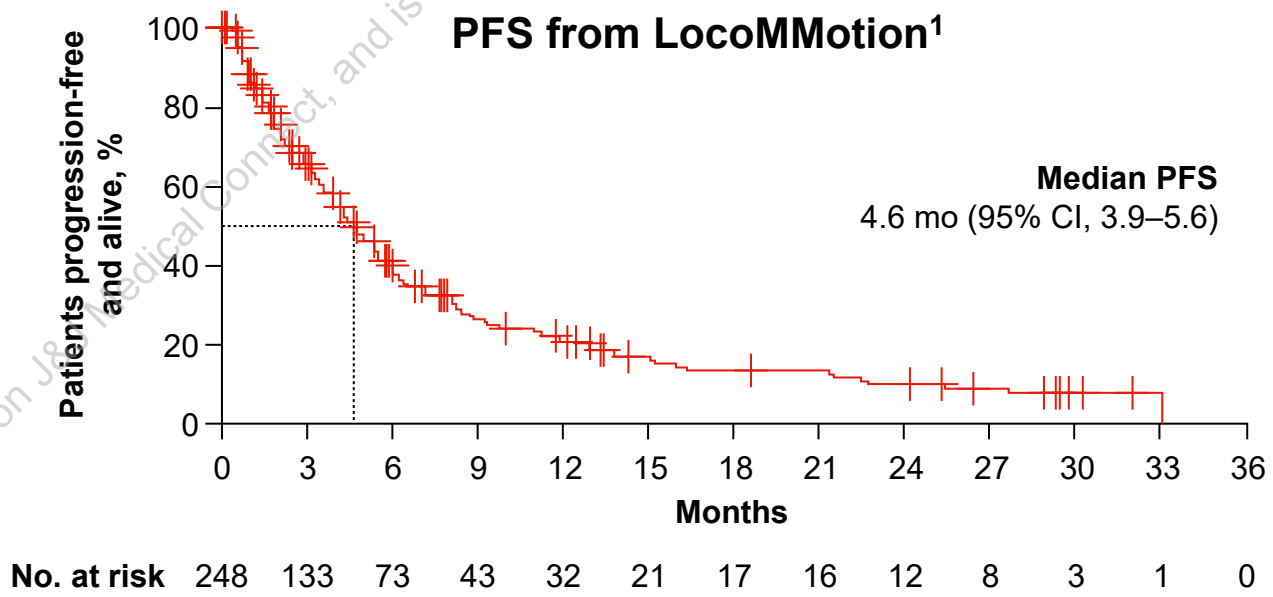
# CARTITUDE-1 Long-Term Remission: Introduction

- Based on RWE from a prospective observational study with similar eligibility criteria, LocoMMotion, the expected median PFS in TCE RRMM was 4.6 months and median OS was ~1 year[1]
- In the CARTITUDE-1[a] study of cilta-cel (BCMA CAR-T), median time to progression on last prior LOT was ~4 months[2]:
  - At a median follow-up of 33.4 months, median PFS was 34.9 months, and median OS was not reached[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; MRD, minimal residual disease; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma; RWE, real-world evidence; TCE, triple-class exposed.
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.





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# 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

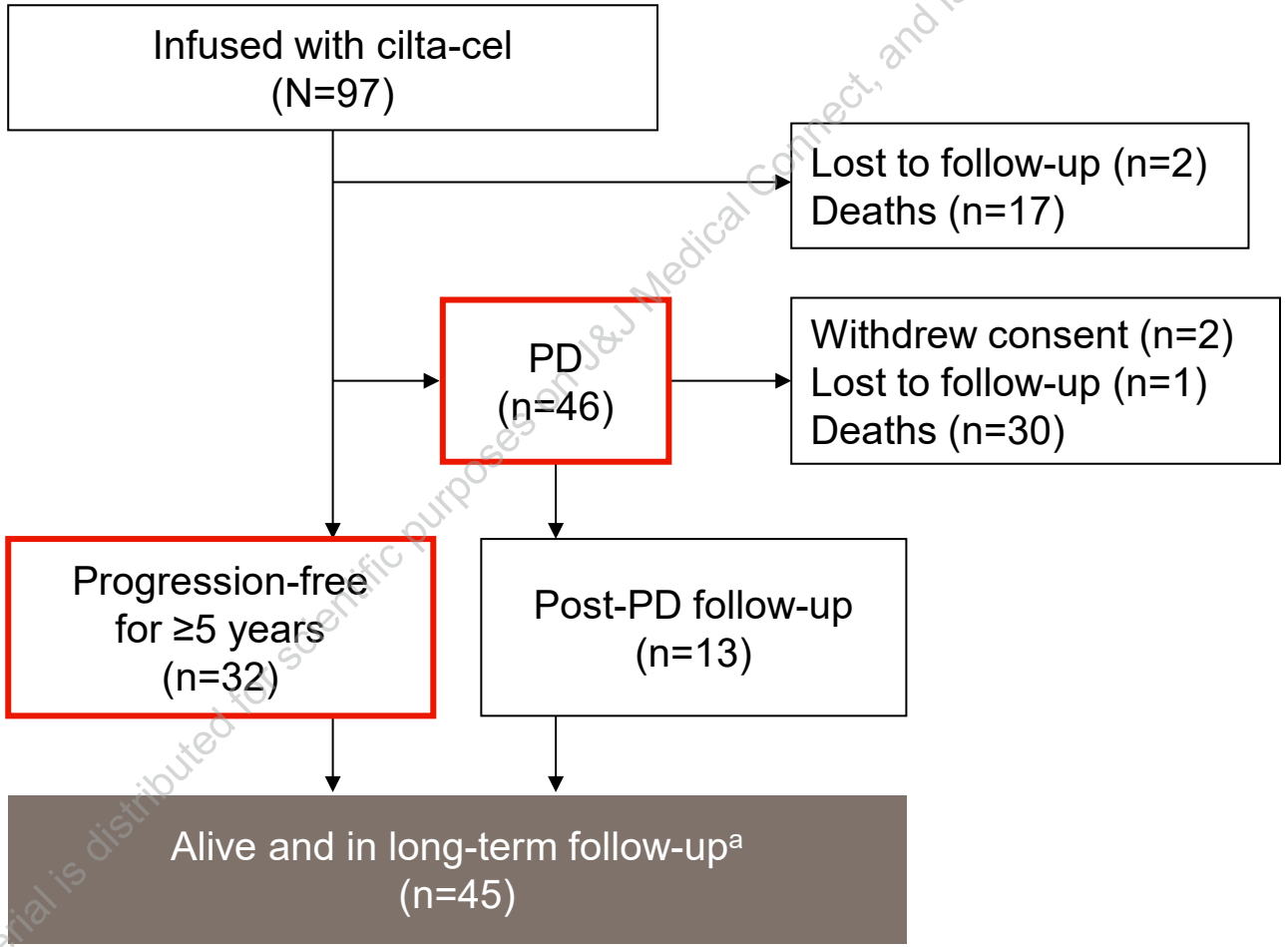
Patient evaluations per local SOC (reported annually at a minimum)

**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; SOC, standard of care.

# CARTITUDE-1 Long-Term Remission: Patient Disposition




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





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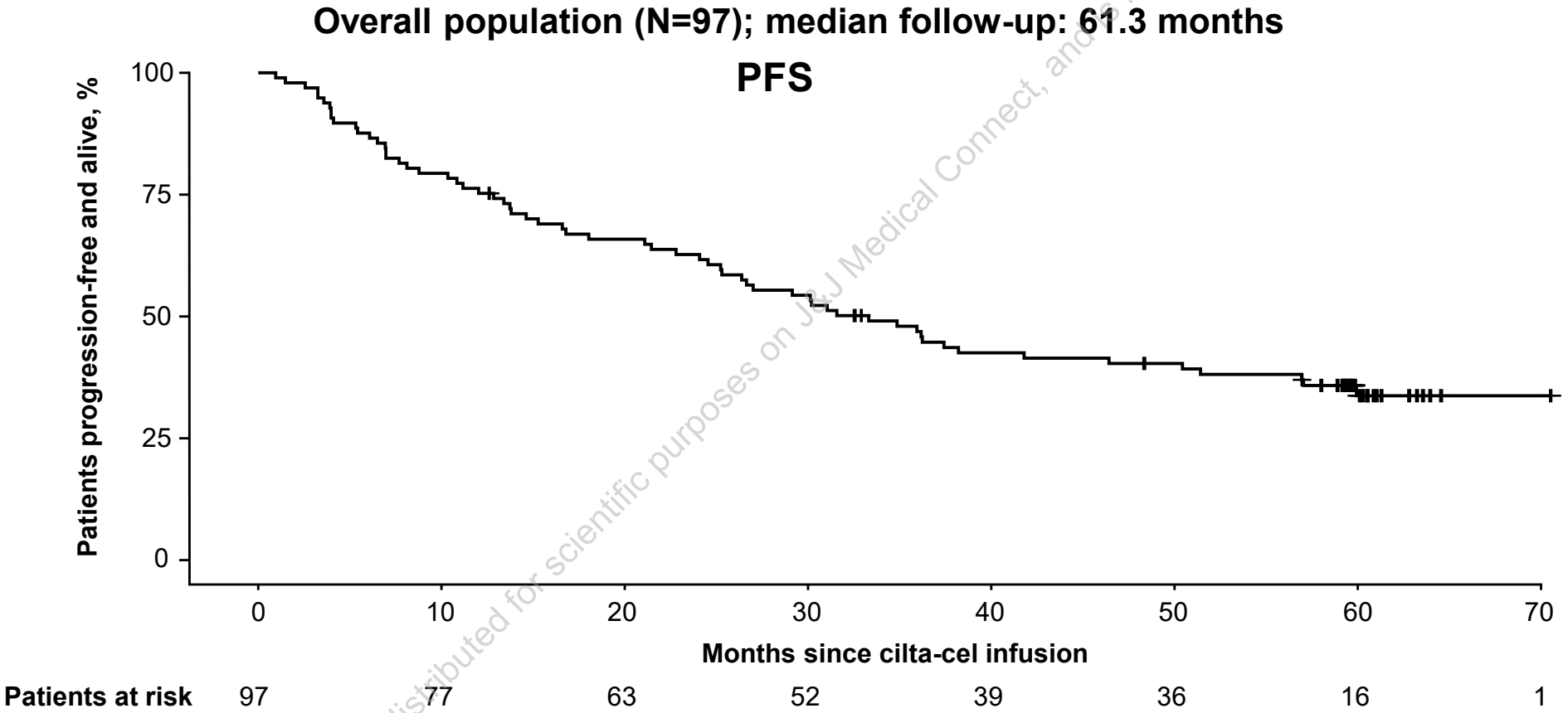
# CARTITUDE-1 Long-Term Remission: One-Third of Patients Were Progression-Free for ≥5 Years




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

cilta-cel, ciltacabtagene autoleucel; PFS, progression-free survival.





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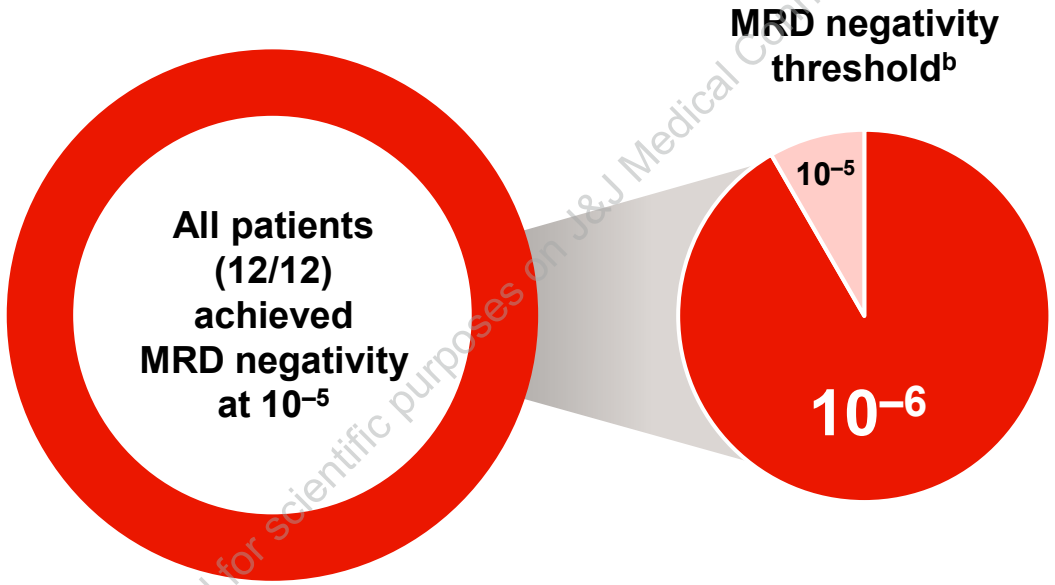
# CARTITUDE-1 Long-Term Remission: Sustained MRD Negativity in All Long-Term Responders at a Single Center

- Of the patients who were progression-free, 12 patients in sCR 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; sCR, stringent complete response.





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# 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 cell <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 cell ≥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.





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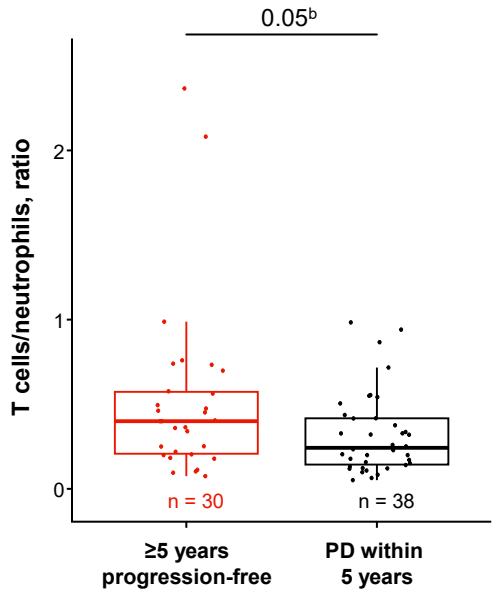
# CARTITUDE-1 Long-Term Remission: Long-Term Disease Control Was Associated With Fitter Immune T Cells Before Infusion and Higher E:T Ratio After Infusion

## Preinfusion

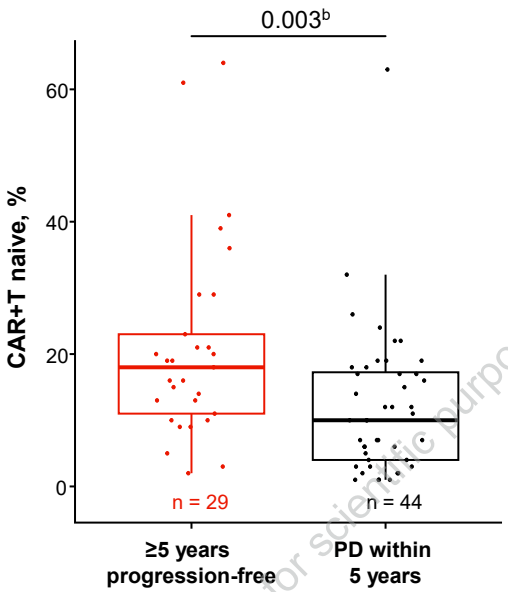
### At apheresis

#### T cells/neutrophils




### Drug product

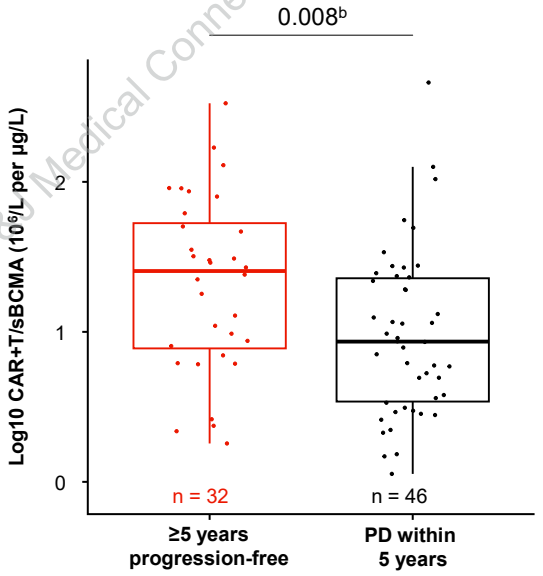
#### CAR+ $T_{naive}$ cells[a]



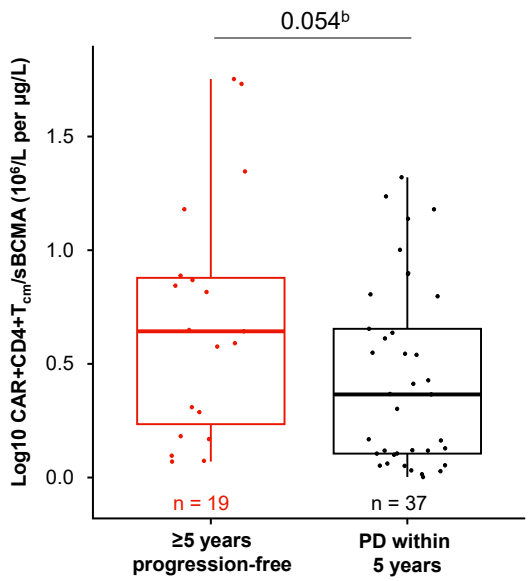

## Postinfusion

### E:T ratio at peak expansion[c]

#### CAR+ T cells




#### CAR+CD4+$T_{cm}$[1]




**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.





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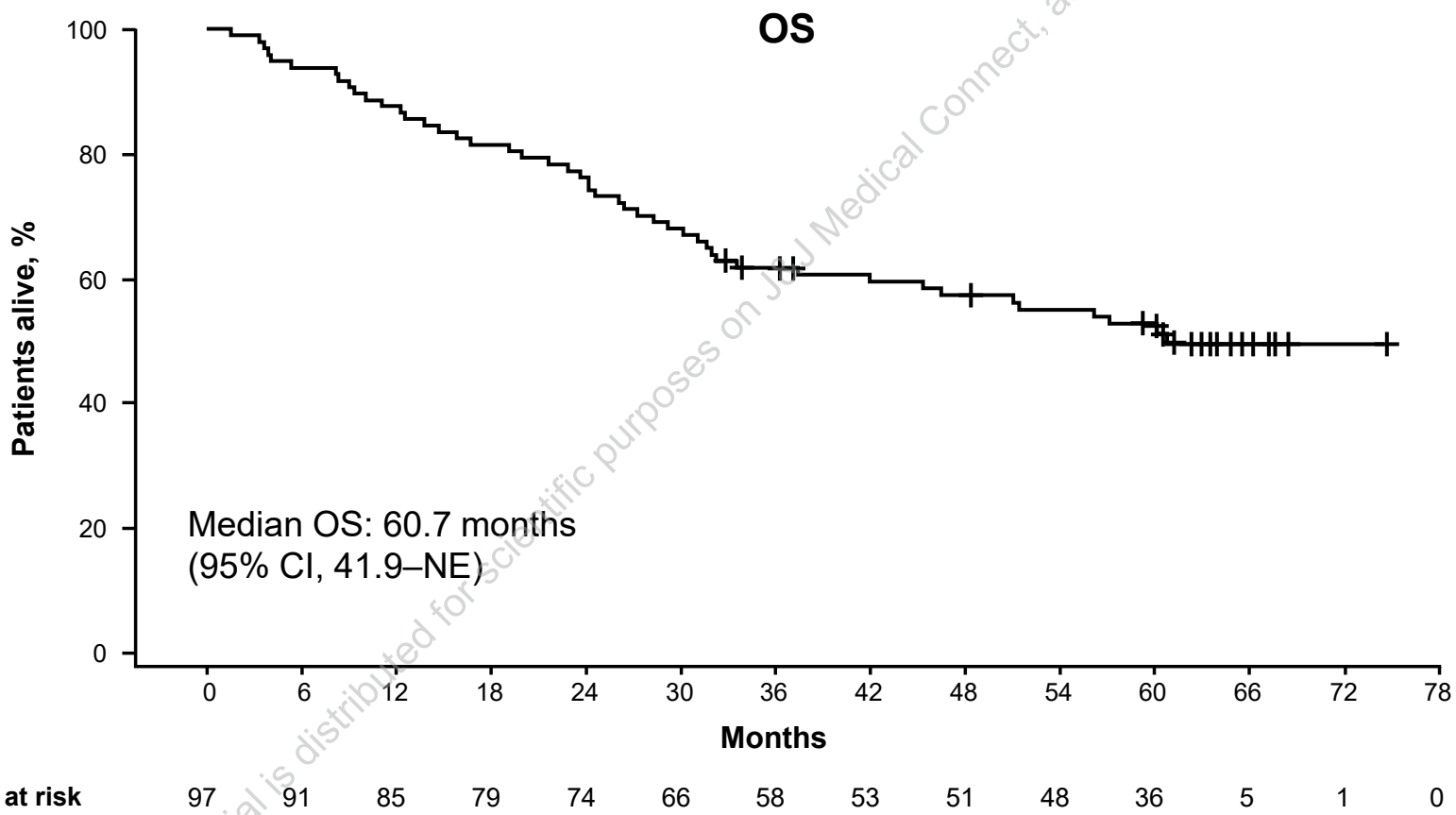
# CARTITUDE-1 Long-Term Remission: Median Overall Survival Was 5 Years

**Overall population (N=97); median follow-up: 61.3 months**




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 transient hepatic 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.



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# CARTITUDE-1 Long-Term Remission: Conclusions

- One-third (33%, n=32) of the patients with a historical median PFS 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 overall survival 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; MRD, minimal residual disease; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma.



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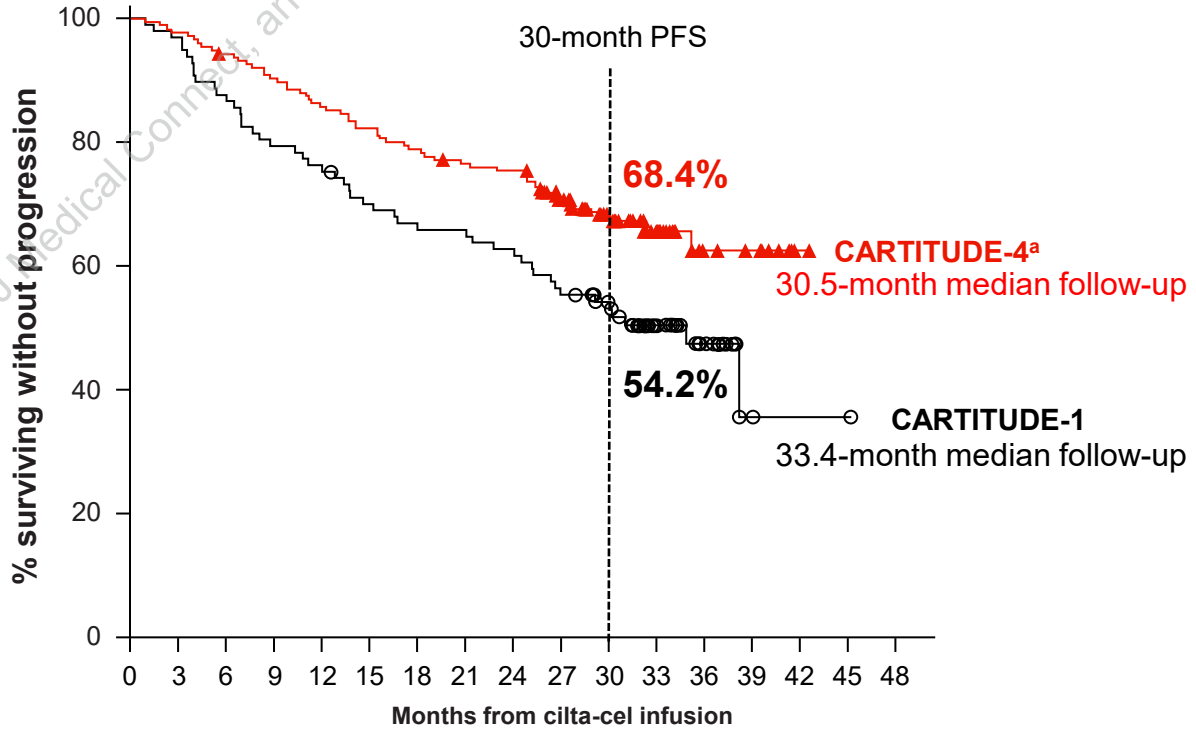
# CARTITUDE-1 Long-Term Remission: Cilta-cel Future Directions

- Earlier use of cilta-cel may further extend long-term remissions due to:
  - Fitter CAR-T cell profiles
  - Improved E:T ratios due to lower tumor burden and effective bridging therapy
- CARTITUDE-5[1] and CARTITUDE-6[2] are evaluating the impact of cilta-cel in NDMM vs SOC with the potential to demonstrate cure and replace transplant (CARTITUDE-6)

**PFS (as-treated population) in patients from CARTITUDE-1 and CARTITUDE-4[a] with similar follow-up[3]**




[a]Re-baselined to begin at time of cilta-cel infusion for patients who received cilta-cel as study treatment, with median follow-up of 30.5 months.
CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; E:T, effector to target; LOT, line of therapy, NDMM, newly diagnosed 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.
3. Mateos MV, et al. Presented at IMS; September 25–28, 2024; Rio de Janeiro, Brazil. Oral #1437





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# Publication

- Simultaneous online publication in the *Journal of Clinical Oncology*
  - S Jagannath, et al. Long-Term (≥5-Year) Remission and Survival After Treatment With Ciltacabtagene Autoleucel in CARTITUDE-1 Patients With Relapsed/Refractory Multiple Myeloma. *JCO* 0, JCO-25-00760; DOI: 10.1200/JCO-25-00760

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