Long-Term Benefits in Patient-Reported Outcomes and Time to Next Antimyeloma Therapy of Ciltacabtagene Autoleucel Versus Standard of Care for Patients With Lenalidomide-Refractory Multiple Myeloma: Results From the Phase 3 CARTITUDE-4 Clinical Trial

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CARTITUDE-4: Introduction

- Earlier use of lenalidomide therapy in MM has led to an increase in patients who are lenalidomide refractory after first relapse[1]
  - HRQoL deteriorates with each relapse and additional LOT[2]
- CARTITUDE-4 evaluated cilta-cel vs SOC in patients with lenalidomide-refractory MM after 1–3 prior LOT[3,4]
  - At median 15.9-month follow-up, a single cilta-cel infusion significantly improved PFS (weighted HR, 0.26; *P*<0.0001) and had a manageable safety profile[3]
  - At median 33.6-month follow-up, cilta-cel significantly prolonged OS, reducing the risk of death vs SOC by 45% (HR, 0.55; *P*=0.0009)[4]
- Here, we report PROs and time to next antimyeloma therapy from patients randomized to cilta-cel vs SOC in CARTITUDE-4 at ~3 years of median follow-up

cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; HRQoL, health-related quality of life; IMiD, immunomodulatory drug; LOT, line of therapy; MM, multiple myeloma; OS, overall survival; PI, proteasome inhibitor; PFS, progression-free survival; PRO, patient-reported outcome; SOC, standard of care.

1. de Arriba de la Fuente F, et al. *Cancers (Basel)* 2022;15:155. 2. Fonseca R, et al. *Clin Lymphoma Myeloma Leuk* 2023;23:426-37. 3. San-Miguel J, et al. *N Engl J Med* 2023;389:335-47. 4. Mateos M-V, et al. *Clin Lymphoma Myeloma Leuk* 2024;24(suppl 2):S290.

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CARTITUDE-4: Study Design and PRO Methods

- CARTITUDE-4 is an ongoing global, randomized, phase 3 study[1]
  - Patients were randomized 1:1 to receive cilta-cel or SOC (PVd or DPd)
  - Primary endpoint was PFS; key secondary endpoints included efficacy, safety, and TTW of symptoms as assessed by the MySIm-Q total symptom scale, which was part of the statistical testing hierarchy among the major efficacy endpoints
  - Changes from baseline in PRO scores were also secondary endpoints
  - PROs scales were assessed at baseline (apheresis for cilta-cel and cycle 1 day 1 for SOC); post-baseline assessments occurred on day 28 postinfusion in the cilta-cel arm, at cycle 4 (DPd) or 5 (PVd) in the SOC arm, and at months 3, 6, 9, 12, 18, 24, 30 or until disease progression

MySIm-Q[2]

- **MM-specific questionnaire**
  - 17 items across 2 subscales (symptom and impact)
- **Symptom subscale (5)**
  - Assesses pain, neuropathy, fatigue, digestive, and cognitive symptom domains
- **Impact subscale (3)**
  - Assesses activity, social, and emotional impact domains

EORTC QLQ-C30[3]

- **Cancer-specific questionnaire**
  - Scores range from 0–100
- **Global health status scale**
- **Symptom scales (3)**
  - Fatigue, nausea and vomiting, pain
- **Functional scales (5)**
  - Physical, role, emotional, cognitive, social
- **Single items (6)**
  - Appetite loss, constipation, diarrhea, dyspnea, financial difficulties, insomnia

Cilta-cel, ciltacabtagene autoleucel; DPd, daratumumab, pomalidomide, and dexamethasone; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer quality of life questionnaire core 30-item; MM, multiple myeloma; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; PFS, progression-free survival; PRO, patient-reported outcome; PVd, pomalidomide, bortezomib, and dexamethasone; SOC, standard of care; TTW, time to worsening.

1. San-Miguel J, et al. *N Engl J Med* 2023;389:335-47. 2. Gries KS, et al. *Value Health* 2021;24:1807-19. 3. Aaronson NK, et al. *J Natl Cancer Inst* 1993;85:365-76.

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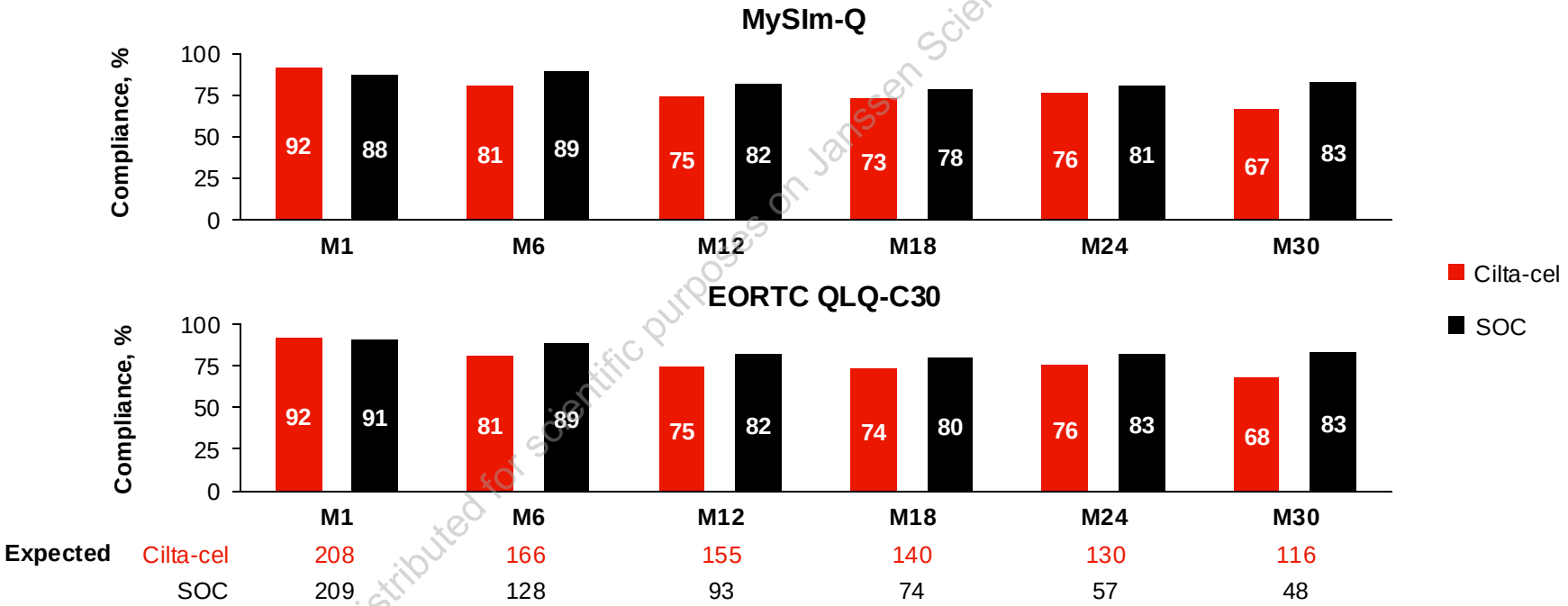
CARTITUDE-4: PRO Compliance Rates Were High

- Compliance rates[a] were generally high for both MySIm-Q and EORTC QLQ-C30 assessments in both treatment arms



Expected		M1	M6	M12	M18	M24	M30
	Cilta-cel	208	166	155	140	130	116
	SOC	209	128	93	74	57	48

[a]Compliance was defined as the number of forms received as a percentage of the number of forms expected.
cilta-cel, ciltacabtagene autoleucel; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer quality of life questionnaire core 30-item; M, month(s); MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; PRO, patient-reported outcome; SOC, standard of care.

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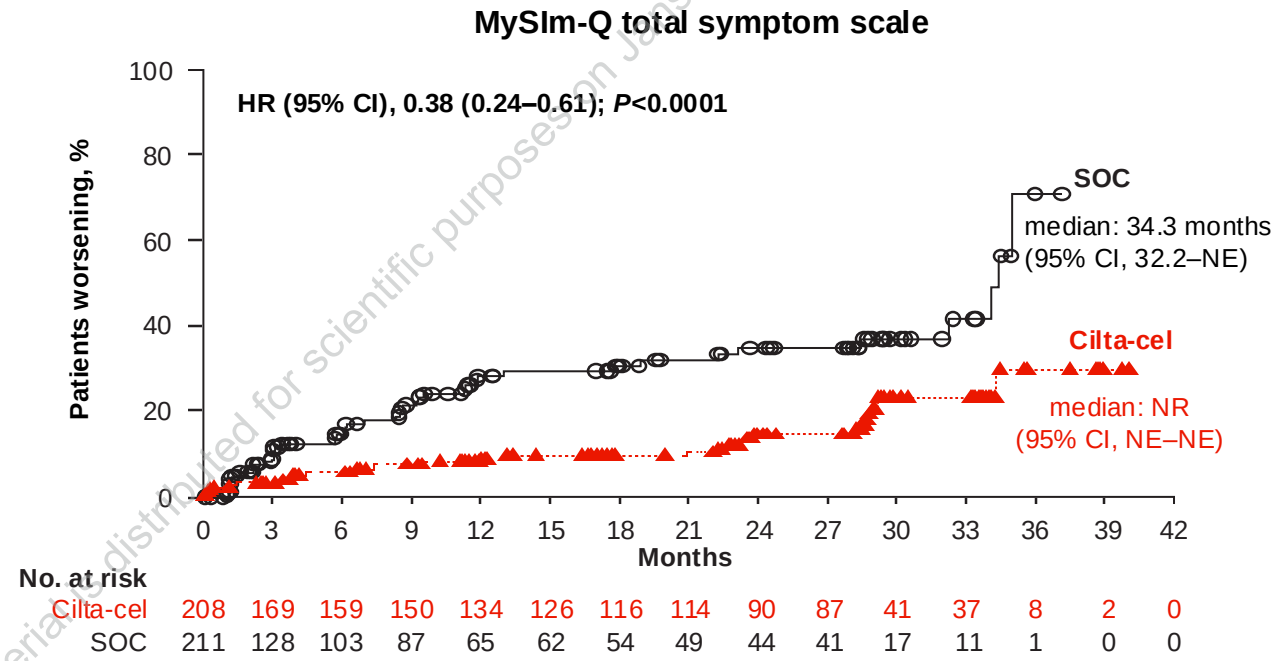
CARTITUDE-4: Time to MySIm-Q Symptom and Impact Worsening Was Significantly Extended With Cilta-cel vs SOC

- Median time until symptom worsening was not reached in the cilta-cel arm and was 34.3 months in the SOC arm
- Median time until impact worsening was 39.2 months (95% CI, 38.7–NE) in the cilta-cel arm and 35.9 months (95% CI, 32.2–NE) in the SOC arm (HR [95% CI], 0.42 [0.26–0.70]; *P*=0.0007)



cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; mTTW, median time to worsening; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; NE, not estimable; NR, not reached; SOC, standard of care.

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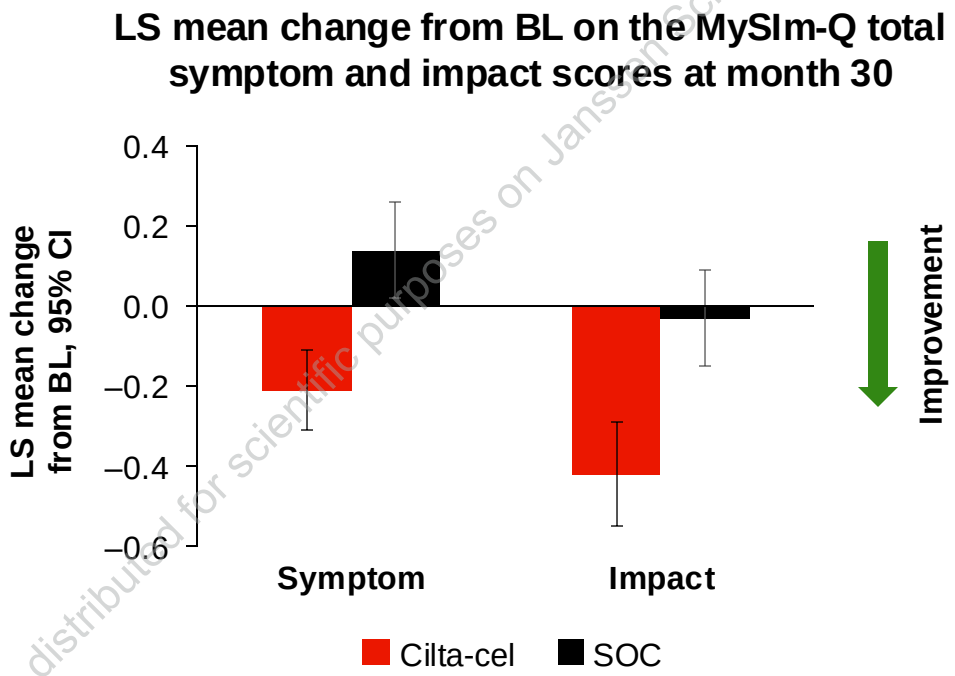
CARTITUDE-4: Improvements in MySIm-Q Total Symptom and Impact Scores Were Higher With Cilta-cel vs SOC

- Least squares mean change from baseline on the MySIm-Q total symptom and impact scores showed greater change with cilta-cel vs SOC at month 30



BL, baseline; cilta-cel, ciltacabtagene autoleucel; LS, least squares; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; SOC, standard of care.

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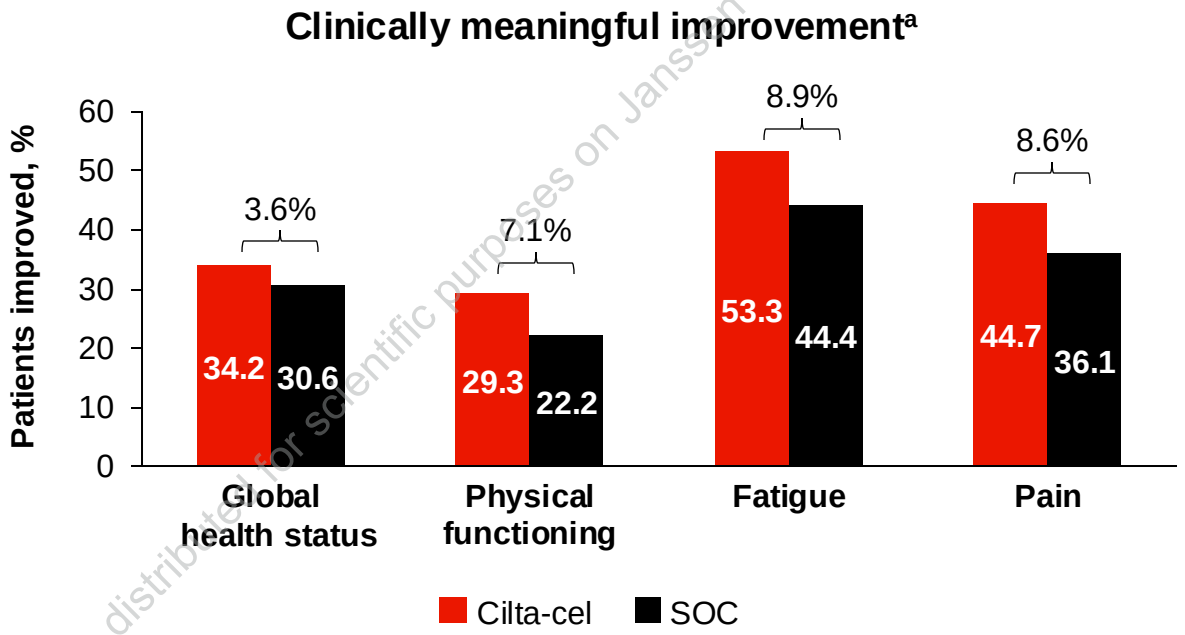
CARTITUDE-4: Clinically Meaningful Improvements in the EORTC QLQ-C30 Global Health Status, Physical Functioning, and Key Symptoms Were Higher With Cilta-cel vs SOC

- Clinically meaningful improvements in global health status, physical functioning, and fatigue and pain symptoms were achieved in a numerically higher proportion of patients in the cilta-cel arm than the SOC arm at month 30



[a]Literature-based minimum importance difference of 10 points was used.
cilta-cel, ciltacabtagene autoleucel; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer quality of life questionnaire core 30-item; SOC, standard of care.

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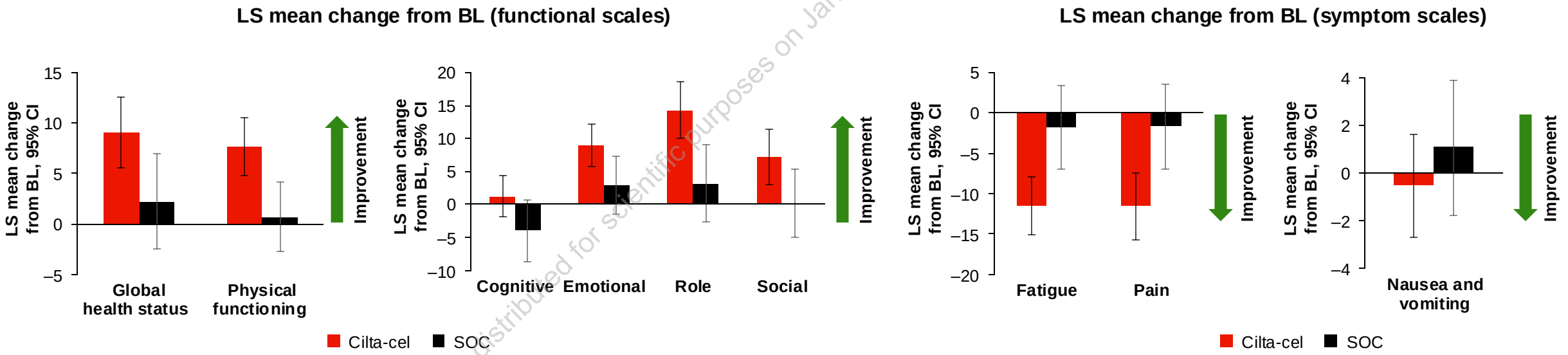
CARTITUDE-4: Greater Improvement in the EORTC QLQ-C30 Functional and Symptom Scales Were Observed With Cilta-cel vs SOC at Month 30

- Least squares mean change from baseline showed greater improvement with cilta-cel vs SOC at month 30 in global health status, physical functioning, and fatigue and pain symptoms
- Cognitive, emotional, role and social functioning, and nausea and vomiting symptoms showed greater improvement in the cilta-cel arm compared with SOC arm



BL, baseline; cilta-cel, ciltacabtagene autoleucel; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer quality of life questionnaire core 30-item; LS, least squares; SOC, standard of care.

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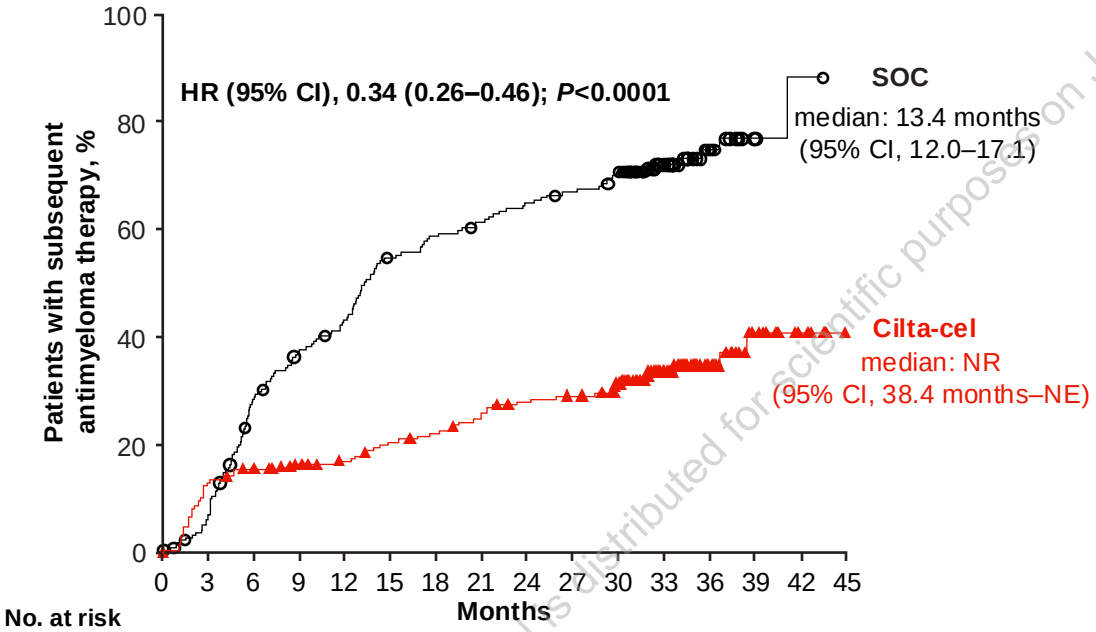
CARTITUDE-4: Time to Next Antimyeloma Therapy Was Significantly Extended With Cilta-cel vs SOC and Treatment-Free Survival Was Not Reached in the Cilta-cel Arm

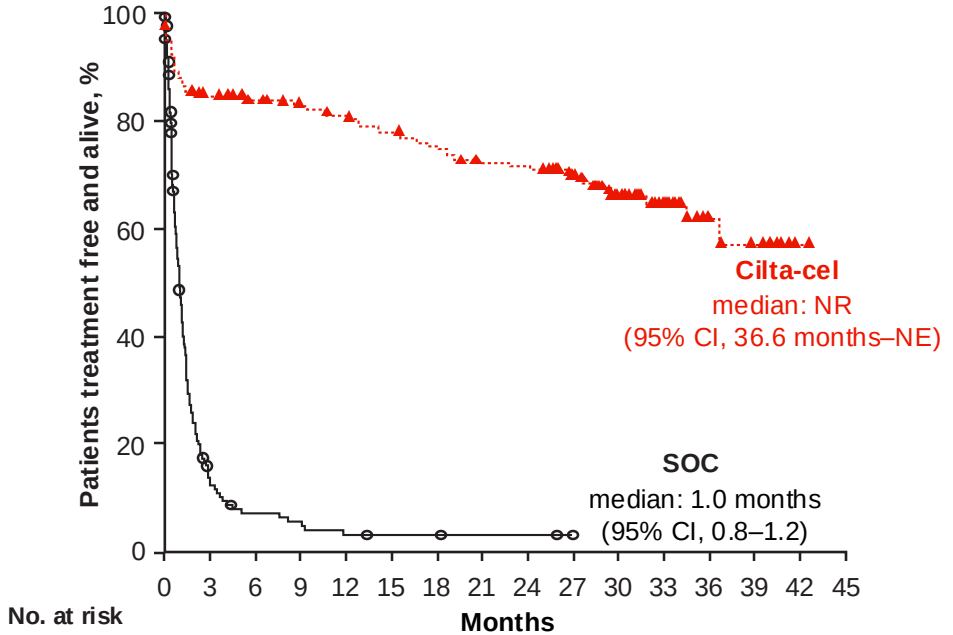
Time to next antimyeloma therapy

- Median time to next antimyeloma therapy was not reached (95% CI, 38.4 months–NE) for cilta-cel, and was 13.4 months (95% CI, 12.0–17.1) for SOC



Treatment-free survival

- Median treatment-free survival was not reached (95% CI, 36.6 months–NE) for cilta-cel, and was 1.0 months (95% CI, 0.8–1.2) for SOC



cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; NE, not estimable; NR, not reached; SOC, standard of care.

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Conclusions

- With ~3 years of follow-up, a single cilta-cel infusion significantly extended time to worsening of MM-related symptoms and functional impacts compared with SOC
- Overall global health status/QoL improved over time in patients in the cilta-cel arm compared with the SOC arm
- A single cilta-cel infusion significantly prolonged time to next antimyeloma therapy compared with continuous SOC treatment, and treatment-free survival was not reached in the cilta-cel arm

Cilta-cel provides prolonged time to next treatment and substantially improves HRQoL, complementing the PFS and OS benefit compared with SOC. Taken together, these benefits support the use of cilta-cel as standard therapy in patients who are lenalidomide-refractory as early as after 1 prior LOT

cilta-cel, ciltacabtagene autoleucel; HRQoL, health-related quality of life; LOT, line of therapy; MM, multiple myeloma; OS, overall survival; PFS, progression-free survival; QoL, quality of life; SOC, standard of care.

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