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# 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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## Key Takeaway

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

## 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

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## Introduction

- Earlier use of lenalidomide therapy in multiple myeloma (MM) has led to an increase in patients who are lenalidomide refractory after first relapse[1]
  - Health-related quality of life (HRQoL) deteriorates with each relapse and additional line of therapy (LOT)[2]
- CARTITUDE-4 evaluated cilta-cel vs standard of care (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 progression-free survival (PFS; weighted hazard ratio [HR], 0.26; *P*<0.0001) and had a manageable safety profile[3]
  - At median 33.6-month follow-up, cilta-cel significantly prolonged overall survival (OS), reducing the risk of death vs SOC by 45% (HR, 0.55; *P*=0.0009)[4]
- Here, we report patient-reported outcomes (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

## Methods

- CARTITUDE-4 is an ongoing global, randomized, phase 3 study[3]
  - Patients were randomized 1:1 to receive cilta-cel or SOC (pomalidomide, bortezomib, and dexamethasone [PVd] or daratumumab, pomalidomide, and dexamethasone [DPd])
  - Primary endpoint was PFS; key secondary endpoints included efficacy, safety, and time to worsening (TTW) of symptoms as assessed by the Multiple Myeloma Symptom and Impact Questionnaire (MySIm-Q) total symptom scale, which was part of the statistical testing hierarchy among the major efficacy endpoints
  - Changes from baseline (BL) in PRO scores were also secondary endpoints
- PROs scales were assessed at BL (apheresis for cilta-cel and cycle 1 day 1 for SOC); post-BL 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 (**Figure 1**)
- TTW of symptoms and impact were defined as the time from randomization to an increase in score of ≥0.5 standard deviation from BL without an observed superior subsequent improvement
  - Patients were censored at last PRO assessment if they had not worsened, or had started subsequent therapy; patients were also censored at randomization if they did not have a BL or ≥1 post-BL PRO assessments
- Least squares (LS) mean changes from BL were evaluated using mixed model for repeated measures

**Figure 1: PRO assessments**

**MySIm-Q[5]**
- **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[6]**
- **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

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer quality of life questionnaire core 30-item.

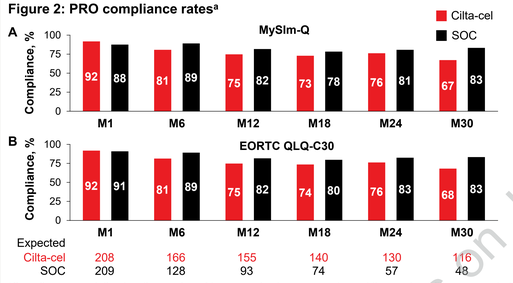
- Time to next antimyeloma therapy was defined as time from randomization to the start of subsequent antimyeloma therapy or death due to progressive disease (PD), whichever comes first
- Treatment-free survival was defined as the duration of time from the date of the last study treatment to subsequent therapy or death due to PD, whichever comes first
- Outcomes were assessed using the Kaplan-Meier method. Stratified Cox proportional hazards models were used to estimate HR and 95% CI

## Results

### PRO compliance

- As of May 2024, median follow-up was 33.6 months (range, 0.1–45.0)
- Compliance rates were generally high for both MySIm-Q and EORTC QLQ-C30 assessments in both treatment arms (**Figure 2**)
  - Main reasons for noncompliance were other (ie, mistakes, forgot, site error/oversight, unknown, site staff not available, administrative failure, used paper, tablet issues) and technical failure

**Figure 2: PRO compliance rates[a]**



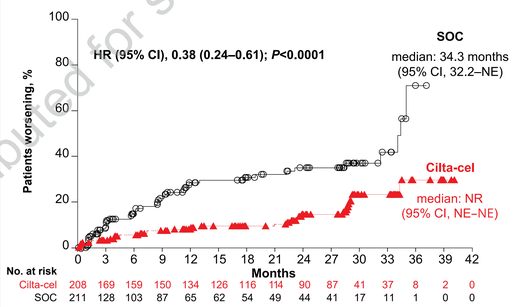

| Expected | M1 | M6 | M12 | M18 | M24 | M30 |
|---|---|---|---|---|---|---|
| Cilta-cel | 208 | 166 | 155 | 140 | 130 | 116 |
| SOC | 209 | 128 | 93 | 74 | 57 | 48 |

[a]Compliance was defined as the number of forms received as a percentage of the number of forms expected. M, month(s).

### MySIm-Q total symptom and impact scales

- Overall, 86% of patients in the cilta-cel arm and 77% in the SOC arm were censored from the MySIm-Q time to sustained worsening analysis
  - Among patients censored, the primary reasons were PD/receipt of subsequent antimyeloma therapy (cilta-cel: 32%; SOC: 64%) and study cut-off (cilta-cel: 57%; SOC: 22%)
- Median time until symptom worsening was not reached (NR) in the cilta-cel arm and was 34.3 months in the SOC arm (**Figure 3**)
  - Event-free rates at 30 months were 77% in the cilta-cel arm and 63% in the SOC arm

**Figure 3: TTW in MySIm-Q total symptom scale**

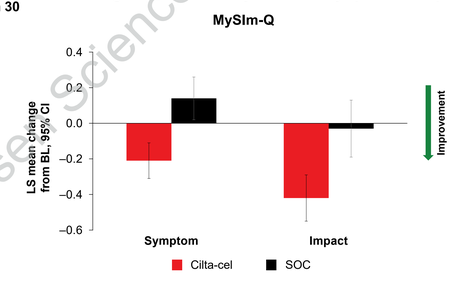



| No. at risk | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cilta-cel | 208 | 169 | 159 | 150 | 134 | 126 | 116 | 114 | 90 | 87 | 41 | 37 | 8 | 2 | 0 |
| SOC | 211 | 128 | 103 | 87 | 65 | 62 | 54 | 49 | 44 | 41 | 17 | 11 | 1 | 0 | 0 |

mTTW, median time to worsening; NE, not estimable.

- 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)
  - Event-free rates at 30 months were 83% in the cilta-cel arm and 69% in the SOC arm
- LS mean change from BL in the MySIm-Q total symptom and impact scores showed greater change with cilta-cel vs SOC at month 30 (**Figure 4**)

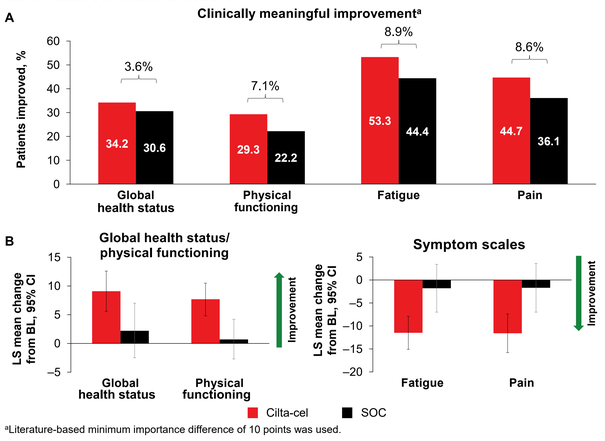
**Figure 4: LS mean change from BL on the MySIm-Q total symptom and impact scores at month 30**




### EORTC QLQ-C30 global health status/quality of life (QoL)

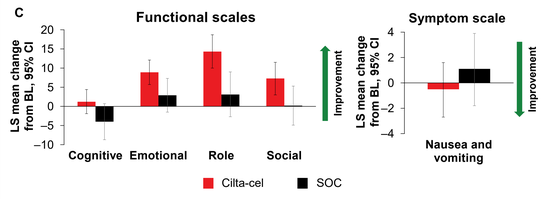
- Clinically meaningful improvements in global health status, physical functioning, and fatigue and pain symptoms were achieved in a numerically higher proportion of patients in the cilta-cel arm than the SOC arm at month 30 (**Figure 5A**)
- LS mean change from BL showed greater improvement with cilta-cel vs SOC at month 30 in global health status, physical functioning, and fatigue and pain symptoms (**Figure 5B**)
  - Cognitive, emotional, role and social functioning, and nausea and vomiting symptoms showed greater improvement in the cilta-cel arm compared with SOC arm (**Figure 5C**)

**Figure 5: (A) Clinically meaningful improvement and (B) LS mean change from BL on EORTC QLQ-C30 scales at month 30**




[a]Literature-based minimum importance difference of 10 points was used.

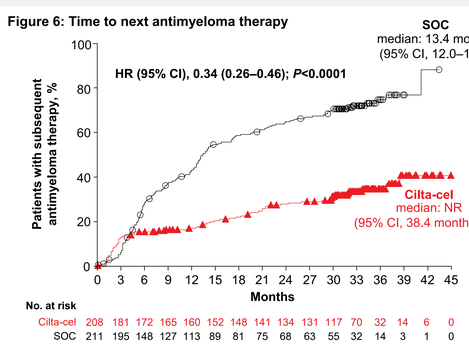
**Figure 5 (continued): (C) LS mean change from BL on EORTC QLQ-C30 scales at month 30**




### Time to next antimyeloma therapy

- Median time to next antimyeloma therapy was NR (95% CI, 38.4 months–NE) for cilta-cel, and was 13.4 months (95% CI, 12.0–17.1) for SOC (**Figure 6**)

**Figure 6: Time to next antimyeloma therapy**

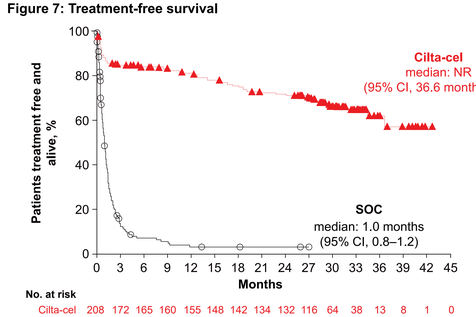



| No. at risk | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cilta-cel | 208 | 181 | 172 | 165 | 160 | 152 | 148 | 141 | 134 | 131 | 117 | 70 | 32 | 14 | 6 | 0 |
| SOC | 211 | 195 | 148 | 127 | 113 | 89 | 81 | 75 | 68 | 63 | 55 | 32 | 14 | 3 | 1 | 0 |

### Treatment-free survival

- Median treatment-free survival was NR (95% CI, 36.6 months–NE) for cilta-cel, and was 1.0 months (95% CI, 0.8–1.2) for SOC (**Figure 7**)

**Figure 7: Treatment-free survival**




| No. at risk | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cilta-cel | 208 | 172 | 165 | 160 | 155 | 148 | 142 | 134 | 132 | 116 | 64 | 38 | 13 | 8 | 1 | 0 |
| SOC | 211 | 19 | 9 | 7 | 4 | 3 | 3 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |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