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Patient-Reported Outcomes in the Phase 3 CARTITUDE-4 Study of Ciltacabtagene Autoleucel vs Standard of Care in Patients With Lenalidomide-Refractory Multiple Myeloma After 1–3 Lines of Therapy

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Key Takeaway

Cilta-cel vs SOC yielded greater improvements in HRQoL that, combined with significant PFS benefit,[5,6] reinforce its potential to be a new SOC for lenalidomide-refractory MM as early as after first relapse

Conclusions

In CARTITUDE-4, a single cilta-cel infusion led to numerically greater improvements on multiple PRO instruments vs SOC

Clinically meaningful improvements were achieved in global health status score at month 12 in a greater proportion of patients in the cilta-cel arm, along with greater improvements in emotional, social, physical, and role functioning than in the SOC arm

Greater improvement in self-reported general health, assessed by EQ-5D-5L visual analogue scale, and reductions in pain and fatigue, assessed by EORTC QLQ-C30, were observed with cilta-cel

Greater improvement in MM symptoms and impacts, assessed by MySIm-Q, were observed with cilta-cel at month 12

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Disclosures

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Introduction

- Ciltacabtagene autoleucel (cilta-cel) is a chimeric antigen receptor (CAR)-T cell therapy approved for the treatment of relapsed/refractory multiple myeloma (RRMM) after ≥4 lines of therapy (LOT) in the US (≥3 LOT in the EU)[1,2]
- In the phase 1b/2 CARTITUDE-1 trial, a single cilta-cel infusion in heavily pretreated patients led to deep and durable responses alongside a manageable safety profile[3]
  - Improved health-related quality of life (HRQoL) was observed, including emotional and physical functioning and reduced multiple myeloma (MM)-related symptoms[4]
- The phase 3 CARTITUDE-4 trial compared cilta-cel with standard of care (SOC) in patients with lenalidomide-refractory MM after 1–3 LOT[5,6]
  - A single cilta-cel infusion significantly improved progression-free survival (PFS) and increased the rate and depth of response vs SOC[5,6]
- Here, we present patient-reported outcomes (PROs) from patients randomized to cilta-cel vs SOC in CARTITUDE-4 at 15.9-month median follow-up

Methods

CARTITUDE-4 (NCT04181827) study design

- 419 patients with lenalidomide-refractory MM and 1–3 prior LOT, including a proteosome inhibitor (PI) and an immunomodulatory drug (IMiD), were randomized to receive either cilta-cel (N=208) or SOC (N=211) (**Figure 1**)
- The primary endpoint was PFS, defined as time from randomization to disease progression/death; while secondary endpoints included efficacy (complete response or better [≥CR], overall response rate [ORR], minimal residual disease [MRD] negativity, and overall survival [OS]), safety, and PROs

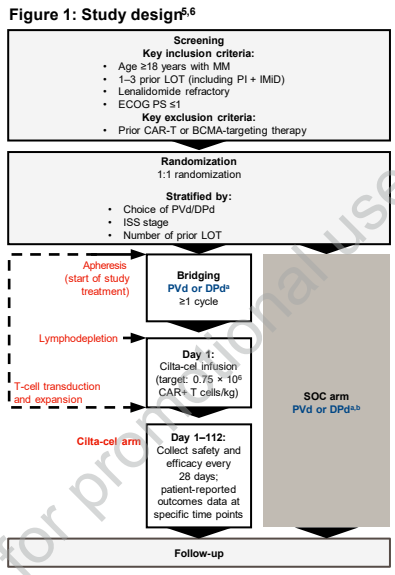
PRO assessments

- PRO assessments were administered at baseline and at months 3, 6, 9, 12, 18, and 24 in both arms
  - Change from baseline was calculated for patients with assessments at baseline and at the given time point
- European Organisation for Research and Treatment of Cancer quality of life questionnaire core 30 (EORTC QLQ-C30; 100-point scale), EuroQoL 5-Dimension 5-Level (EQ-5D-5L; 100-point scale), and Multiple Myeloma Symptom and Impact Questionnaire (MySIm-Q; 5-point scale) questionnaires were administered to all patients until disease progression
  - EORTC QLQ-C30[7] is a cancer-specific questionnaire, measuring global health status
    - 3 symptom scales: fatigue, nausea and vomiting, and pain
    - 5 functional scales: physical, role, emotional, cognitive, and social
  - EQ-5D-5L[8] is a generic measurement of health, consisting of a visual analogue scale and was collected post disease progression every 16 weeks until end of study
    - Patients self-rate their health between 100 (best imaginable health) and 0 (worst imaginable health)
  - MySIm-Q[9] is a MM-specific questionnaire, assessing 17 single items across 8 domains on a 5-point verbal scale
    - Symptom subscale: pain, neuropathy, fatigue, digestive, and cognitive symptom domains
    - Impact subscale: activity, social, and emotional impact domains

Statistical analysis

- PRO compliance was calculated as the number of patients whose PROs were received divided by the whose PROs were expected
- Mixed-model for repeated measures analyses were performed to analyze changes from baseline for each arm and included the baseline PRO score and prognostic characteristics as covariates to balance arms and adjust for confounders
- Time to symptom worsening, defined as a clinically meaningful increase (≥0.5 SD of pooled baseline values) without a subsequent reduction in MM symptoms, was assessed using the Kaplan-Meier method

Figure 1: Study design[5,6]



[a]Physicians' choice. [b]Administered until disease progression.
BCMA, B-cell maturation antigen; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; PVd, pomalidomide, bortezomib, and dexamethasone.

Results

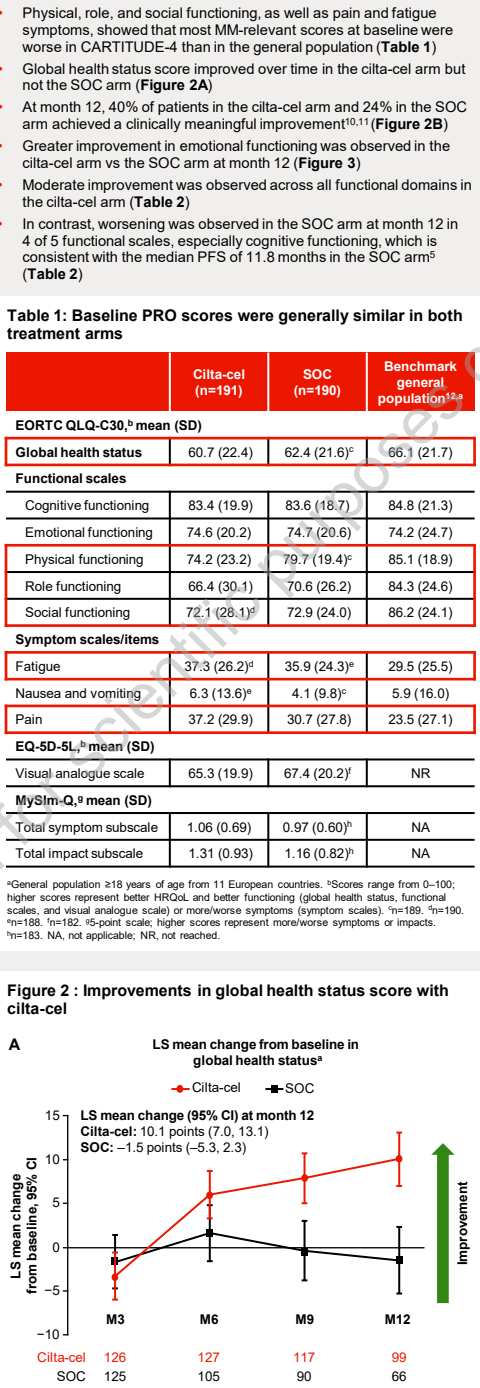
- Compliance rates were high and decreased over time for EORTC QLQ-C30
  - In general, a similar trend was observed with compliance rates for EQ-5D-5L and MySIm-Q
- Global health status scores at baseline for both treatment arms were lower than benchmark scores for the general population, suggesting worse overall health (**Table 1**)
- Physical, role, and social functioning, as well as pain and fatigue symptoms, showed that most MM-relevant scores at baseline were worse in CARTITUDE-4 than in the general population (**Table 1**)
- Global health status score improved over time in the cilta-cel arm but not the SOC arm (**Figure 2A**)
- At month 12, 40% of patients in the cilta-cel arm and 24% in the SOC arm achieved a clinically meaningful improvement[10,11] (**Figure 2B**)
- Greater improvement in emotional functioning was observed in the cilta-cel arm vs the SOC arm at month 12 (**Figure 3**)
- Moderate improvement was observed across all functional domains in the cilta-cel arm (**Table 2**)
- In contrast, worsening was observed in the SOC arm at month 12 in 4 of 5 functional scales, especially cognitive functioning, which is consistent with the median PFS of 11.8 months in the SOC arm[5] (**Table 2**)

Table 1: Baseline PRO scores were generally similar in both treatment arms

	Cilta-cel (n=191)	SOC (n=190)	Benchmark general population[12a]
EORTC QLQ-C30,[b] mean (SD)			
Global health status	60.7 (22.4)	62.4 (21.6)[c]	66.1 (21.7)
Functional scales			
Cognitive functioning	83.4 (19.9)	83.6 (18.7)	84.8 (21.3)
Emotional functioning	74.6 (20.2)	74.7 (20.6)	74.2 (24.7)
Physical functioning	74.2 (23.2)	79.7 (19.4)[c]	85.1 (18.9)
Role functioning	66.4 (30.1)	70.6 (26.2)	84.3 (24.6)
Social functioning	72.1 (28.1)[d]	72.9 (24.0)	86.2 (24.1)
Symptom scales/items			
Fatigue	37.3 (26.2)[d]	35.9 (24.3)[e]	29.5 (25.5)
Nausea and vomiting	6.3 (13.6)[e]	4.1 (9.8)[c]	5.9 (16.0)
Pain	37.2 (29.9)	30.7 (27.8)	23.5 (27.1)
EQ-5D-5L,[b] mean (SD)			
Visual analogue scale	65.3 (19.9)	67.4 (20.2)[f]	NR
MySIm-Q,[9] mean (SD)			
Total symptom subscale	1.06 (0.69)	0.97 (0.60)[h]	NA
Total impact subscale	1.31 (0.93)	1.16 (0.82)[h]	NA

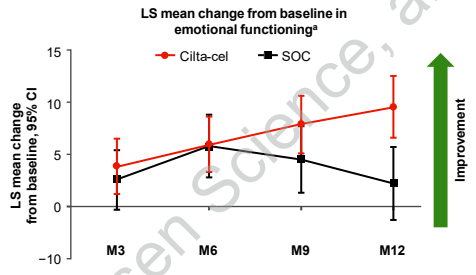
[a]General population ≥18 years of age from 11 European countries. [b]Scores range from 0–100; higher scores represent better HRQoL and better functioning (global health status, functional scales, and visual analogue scale) or more/worse symptoms (symptom scales). [c]n=189. [d]n=190. [e]n=188. [f]n=182. [g]5-point scale; higher scores represent more/worse symptoms or impacts. [h]n=183. NA, not applicable; NR, not reached.

Figure 2 : Improvements in global health status score with cilta-cel



[a]Mixed-model for repeated measures analyses were conducted using data from patients with assessments at both baseline and the given time point. Baseline PRO score and prognostic characteristics were included as covariates to balance arms and to adjust for confounders. Assessments after the start of subsequent therapy were excluded. [b]Change from baseline ≥10 points. LS, least squares; M, month.

Figure 3: Improvements in most functional scales with cilta-cel



[a]Mixed-model for repeated measures analyses were conducted using data from patients with assessments at both baseline and the given time point. Baseline PRO score and prognostic characteristics were included as covariates to balance arms and to adjust for confounders. Assessments after the start of subsequent therapy were excluded.

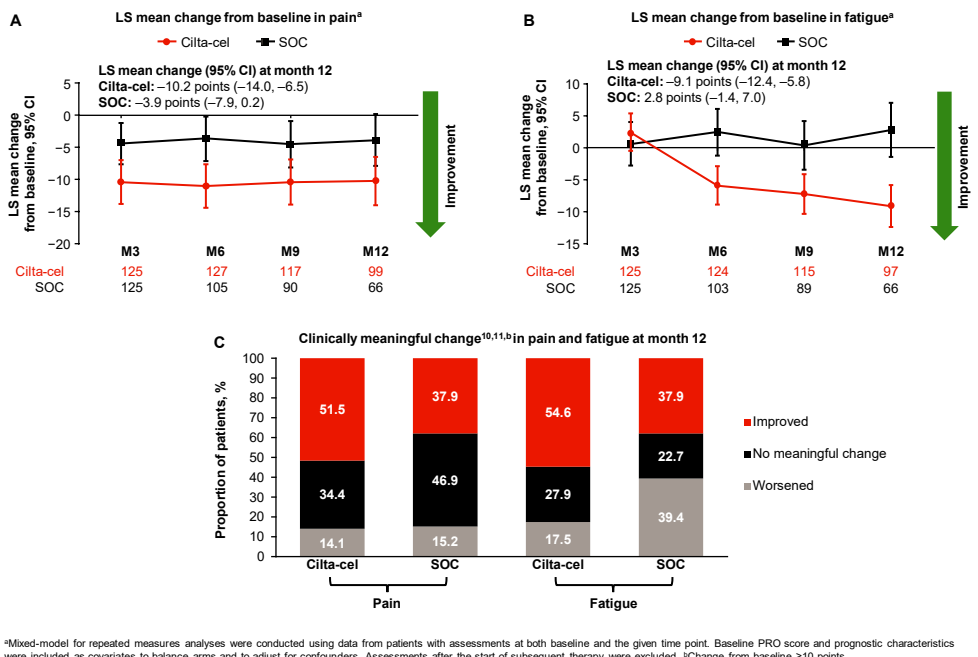
TABLE 2: EORTC QLQ-C30 functional scale change from baseline at month 12[a]

Scale	LS mean change (95% CI)	
	Cilta-cel (n=99)	SOC (n=66)
EORTC QLQ-C30 functional scales		
Cognitive functioning	0.5 (–2.4, 3.5)	–7.5 (–11.2, –3.9)
Emotional functioning	9.5 (6.6, 12.5)	2.2 (–1.3, 5.7)
Physical functioning	6.5 (3.8, 9.1)	–2.1 (–5.0, 0.7)
Role functioning	7.7 (3.7, 11.7)	–1.7 (–6.3, 2.9)
Social functioning	6.1 (2.1, 10.0)	–0.1 (–4.2, 4.0)

Green indicates improvement; dark gray indicates worsening. [a]Mixed-model for repeated measures analyses were conducted using data from patients with assessments at both baseline and the given time point. Baseline PRO score and prognostic characteristics were included as covariates to balance arms and to adjust for confounders. Assessments after the start of subsequent therapy were excluded.

- Mean improvements in pain symptoms in the cilta-cel arm vs the SOC arm were greater at months 3–12, and fatigue symptoms improved over time in the cilta-cel arm but not the SOC arm (**Figure 4A**, **4B**)
- Nausea and vomiting scores changed minimally from baseline in both arms (LS mean change [95% CI] at month 12: cilta-cel, –1.2 [–3.1, 0.7]; SOC, 0.6 [–1.4, 2.7])
- Visual analogue scale score improved over time in the cilta-cel arm but not the SOC arm (data not shown)
  - At month 12, 51% of patients in the cilta-cel arm and 31% in the SOC arm had clinically meaningful[12] improvements in visual analogue scale scores
- Improvements on the MySIm-Q total symptom and total impact subscales were observed in the cilta-cel arm; scores worsened or were near baseline in the SOC arm (**Figure 5A**)
- Median time to sustained symptom worsening was 23.7 months in the cilta-cel arm vs 18.9 months in the SOC arm[5] (**Figure 5B**)

Figure 4: Reduction in pain and fatigue symptoms with cilta-cel over time



[a]Mixed-model for repeated measures analyses were conducted using data from patients with assessments at both baseline and the given time point. Baseline PRO score and prognostic characteristics were included as covariates to balance arms and to adjust for confounders. Assessments after the start of subsequent therapy were excluded. [b]Change from baseline ≥10 points.

Figure 5: Cilta-cel reduced symptoms and impact of MM and delayed time to symptom worsening

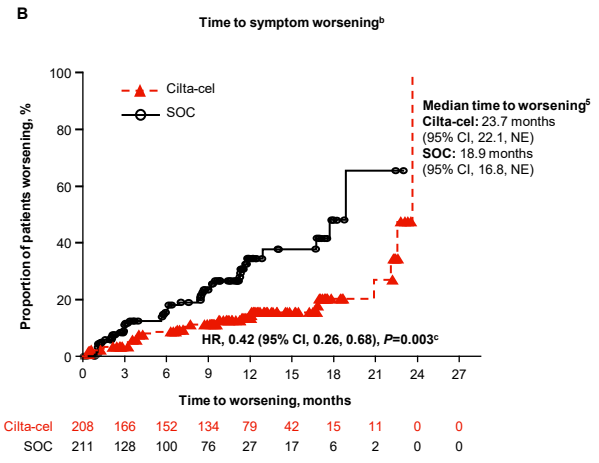
A

Mean change in MySIm-Q from baseline to month 12[a]

Scale	LS mean change (95% CI)	
	Cilta-cel (n=99)	SOC (n=64)
MySIm-Q		
Total symptom subscale	–0.18 (–0.27, –0.10)	0.17 (0.06, 0.27)
Total impact subscale	–0.41 (–0.53, –0.29)	0.01 (–0.13, 0.14)

Green indicates improvement; dark gray indicates worsening. [a]Mixed-model for repeated measures analyses were completed for patients with data from both baseline and the assessed time point. Baseline PRO score and prognostic characteristics were included as covariates to balance arms and to adjust for confounders. Assessments after the start of subsequent therapy were excluded. [b]Defined as an increase (≥0.5 SD of pooled baseline values) without a subsequent reduction in score. [c]Nominal *P* value. NE, not estimable.

B



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