PA-102

Quality-Adjusted Survival Analysis of Cilta-cel vs Standard of Care in Lenalidomide-Refractory Multiple Myeloma Patients Who Received 1–3 Prior Lines of Therapy: CARTITUDE-4 Trial Population

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Key Takeaway

Cilta-cel demonstrated a statistically significant and clinically meaningful gain of time without symptoms or toxicity vs SOC, further supporting its favorable benefit-risk profile in patients with lenalidomide-refractory multiple myeloma

Conclusions

- Patients treated with cilta-cel (in the ITT or as-treated populations) vs SOC experienced a 7.7- to 11.7-month longer duration of time without symptoms or toxicity, representing a 32.1–49.2% relative gain
- The relative survival gain seen with cilta-cel exceeded the 10–15% threshold generally considered clinically important, with higher gains (49.2%) seen in the cilta-cel as-treated population, reinforcing the unprecedented benefit seen with cilta-cel vs SOC
- This benefit was primarily driven by significantly longer PFS time without grade 3/4 AEs (TWiST) in the cilta-cel vs SOC arm (26.2 vs 15.4 months)

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Poster

https://www.congresshub.com/Oncology/IMS2025/Cilta-cel-Sidana

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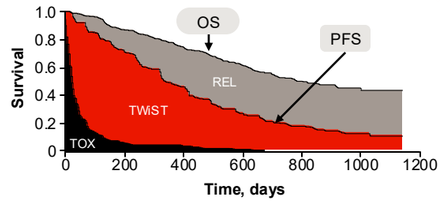
Introduction

- In CARTITUDE-4 (NCT04181827), a single cilta-cel infusion significantly prolonged progression-free survival (PFS) and overall survival (OS) in patients with lenalidomide-refractory multiple myeloma after 1–3 prior lines of therapy[1,2]
- Quality-Adjusted Time Without Symptoms or Toxicity Analysis (Q-TWiST) is a validated method comprehensively integrating progression, survival, treatment toxicities, and patient quality of life into a single metric to evaluate overall treatment effect[3]
- In this analysis, the Q-TWiST method was applied to evaluate the comprehensive benefit-risk profile of cilta-cel vs standard of care (SOC) using data from the CARTITUDE-4 trial

Methods

- As of the May 1, 2024, data cutoff, the Q-TWiST analysis included the intent-to-treat (ITT; cilta-cel [N=208]; SOC [N=211]) and the as-treated (ie, received cilta-cel as study treatment; cilta-cel, [N=176]; SOC, [N=211]) populations from CARTITUDE-4 with a maximum follow-up of 45 months

Figure 1: Partitioned OS curve with progression and toxicity states (TWiST, TOX, and REL)



- Consistent with Q-TWiST methodology, survival time was divided into 3 general, distinct health states (**Figure 1**): PFS time without symptoms or grade 3/4 adverse events (AEs; TWiST), PFS time with symptoms and grade 3/4 AEs (TOX), and time after disease progression (REL)
- Conventional utilities were used for each health state: TWiST (1.0), TOX (0.5), and REL (0.5) (**Figure 2**)
- The base case analysis was conducted in the ITT and as-treated populations and used grade 3/4 (treatment-emergent and non–treatment-emergent) AEs
- A sensitivity analysis was repeated in the ITT and as-treated populations using an alternative AE definition that included grade 1–4 second primary malignancies (SPMs)
- A 10–15% relative Q-TWiST gain was considered as a clinically important difference, based on previous recommendations[4]

Figure 2: Q-TWiST formula with utility weights across health states

$$\text{Q-TWiST} = (U_{\text{TWiST}} \times \text{TWiST}) + (U_{\text{TOX}} \times \text{TOX}) + (U_{\text{REL}} \times \text{REL})$$

Utility value at each health state

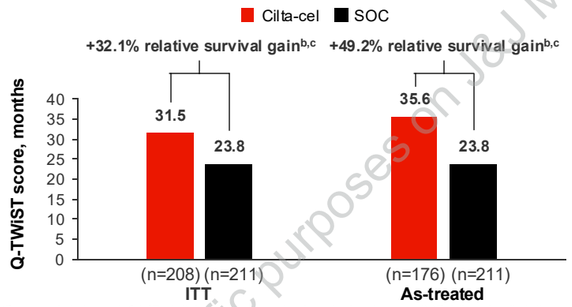
REL, time after disease progression; TOX, PFS time with symptoms and grade 3/4 AEs; TWiST, PFS time without symptoms or grade 3/4 AEs; U, utility value assigned to each health state.

Results

Base case analysis

- Differences were observed across health states between treatment arms in the ITT population (**Table**)
  - Mean PFS time without grade 3/4 AEs was 26.2 months for cilta-cel vs 15.4 months for SOC
- Cilta-cel vs SOC demonstrated a statistically significant improvement in time without symptoms or grade 3/4 AEs in both the ITT and as-treated populations (**Figure 3**)
  - In the ITT population, cilta-cel showed a +32.1% relative gain in time without symptoms or toxicity vs SOC (+7.7 months; 95% CI, 4.8–10.5; *P*<0.001)
  - In the as-treated population, the relative gain in time without symptoms or toxicity was +49.2% in favor of cilta-cel (+11.7 months; 95% CI, 9.1–14.3; *P*<0.001)

Figure 3: Q-TWiST scores for cilta-cel vs SOC in the base case[a] (ITT and as-treated populations)



[a]Base case includes grade 3/4 AEs (both treatment-emergent and non–treatment-emergent). [b]Relative gain reflects the percentage increase in PFS time without symptoms or toxicity with cilta-cel vs SOC. [c]*P*<0.001. Utility weights applied were 1.0 for TWiST and 0.5 for both TOX and REL.

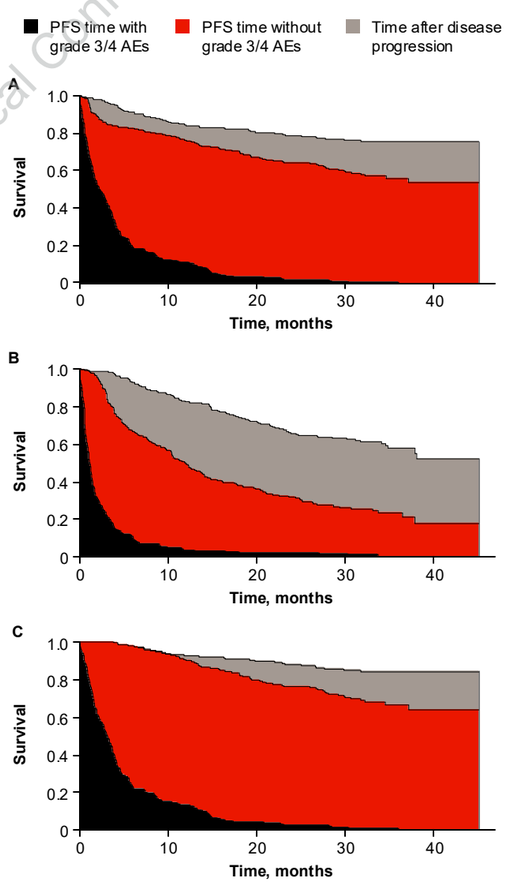
Table: Base case outcomes across Q-TWiST health states for cilta-cel vs SOC in the ITT population

	Cilta-cel	SOC	Cilta-cel vs SOC
	Restricted mean (95% CI)	Restricted Mean (95% CI)	Restricted mean (95% CI)
PFS time with Grade 3/4 AEs	4.3 (3.6, 5.1)	2.4 (1.9, 3.0)	1.9 (0.9, 2.9)
PFS time without Grade 3/4 AEs	26.2 (23.7, 28.6)	15.4 (13.2, 17.7)	10.7 (7.5, 13.9)
Time after disease progression	6.4 (4.8, 8.0)	14.3 (12.2, 16.5)	–8.0 (–10.6, –5.3)
Gain in time without symptoms or Grade 3/4 AEs	**31.5 (29.4, 33.6)**	**23.8 (21.9, 25.8)**	**7.7 (4.8, 10.5)[a]**

[a]*P*<0.001. Base case includes grade 3/4 AEs (both treatment-emergent and non–treatment-emergent). Utility weights applied were 1.0 for TWiST and 0.5 for both TOX and REL.

- A greater proportion of time was spent progression free without grade 3/4 AEs in the cilta-cel arm compared with SOC (**Figure 4**)

Figure 4: Survival curves by Q-TWiST health states for (A) cilta-cel (ITT), (B) SOC (ITT and as-treated), (C) and cilta-cel (as-treated)



ITT and as-treated populations included grade 3/4 AEs (both treatment-emergent and non–treatment-emergent).

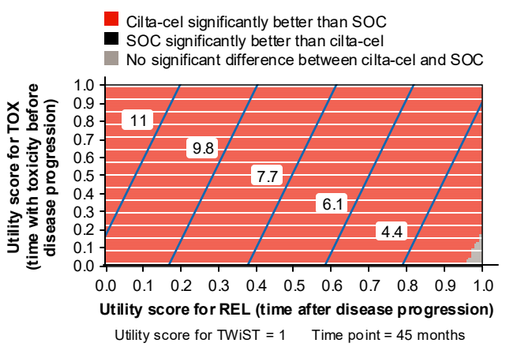
Sensitivity analysis

- When the full range of utility values (0–1) for TOX and REL health states was tested over the maximum follow-up of 45 months, Q-TWiST was statistically higher for cilta-cel vs SOC in most cases (**Figure 5**)
- In the sensitivity analysis, cilta-cel was associated with a significantly longer duration of PFS without grade 3/4 AEs and grade 1–4 SPMs vs SOC in both the ITT and as-treated populations
  - In the ITT population, cilta-cel showed a +7.6-month gain vs SOC (31.4 months vs 23.8 months; *P*<0.001), corresponding to a +32.0% relative gain in time without grade 3/4 AEs and grade 1–4 SPMs vs SOC
  - In the as-treated population, cilta-cel demonstrated an +11.6-month gain vs SOC (35.4 months vs 23.8 months; *P*<0.001), representing a +48.9% relative gain in time without grade 3/4 AEs and grade 1–4 SPMs

Strengths and limitations

- The Q-TWiST method provides a comprehensive, patient-centric evaluation of treatment benefit by integrating survival, toxicity, and progression while accounting for the impact of treatment-related toxicities on quality of life
- A key limitation is the assumption that all grade 3/4 AEs have equal impact on quality of life; this may be addressed by refining TOX state definitions using subsets of AEs with known quality of life impact
- The analysis relied on predefined, fixed utility values originally suggested by Gelber et al. (1995) when introducing the Q-TWiST method[5]
  - Although these value sets are consistent with those used in prior published Q-TWiST studies,[6] validating results using patient-derived utility data from clinical trials or real-world settings would strengthen generalizability
- Results are based on a single data cut (May 1, 2024; median follow-up, 34 months)
- Q-TWiST values may evolve with longer follow-up, potentially showing further benefit for cilta-cel

Figure 5: Q-TWiST estimates for utility values of TOX and REL in the sensitivity analysis[a]



Utility score for TWiST = 1 Time point = 45 months

[a]Numbers shown are Q-TWiST gain over follow-up time of 45 months in the ITT population.

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Multiple Myeloma

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