PA-010

Efficacy/Safety of Cilta-cel ± Lenalidomide Maintenance in Patients With Multiple Myeloma Who Had Suboptimal Response to Frontline ASCT: Updated Follow-Up From CARTITUDE-2 Cohort D

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Key Takeaway

In patients with <CR after frontline ASCT, CARTITUDE-2 cohort D showed that at median ~3.5 years of follow-up, a single cilta-cel infusion led to deep, durable responses, with no new safety signals, in a population with historically poor clinical outcomes

Conclusions

All 16 responders achieved sCR (of 17 treated with cilta-cel ± lenalidomide maintenance), and responses were durable (1 patient had disease progression)

AEs were consistent with the known safety profile of cilta-cel, and no new safety signals were observed at this longer follow-up

In this early MM patient population, the benefit-to-risk ratio of cilta-cel continues to be favorable

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Poster

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Disclosures

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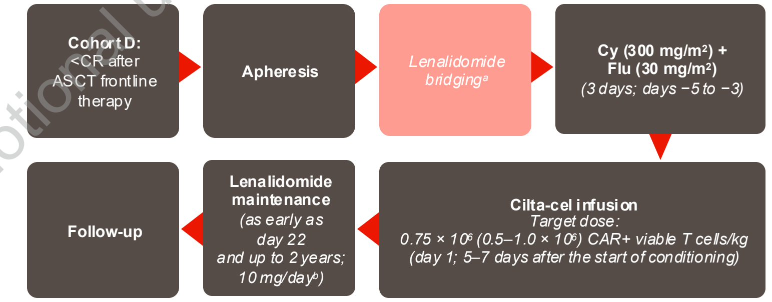
Introduction

- Ciltacabtagene autoleucel (cilta-cel), a B-cell maturation antigen–targeting chimeric antigen receptor (CAR)-T cell therapy, led to deep responses and significant progression-free survival (PFS) and overall survival (OS) benefits vs standard of care in patients with lenalidomide-refractory multiple myeloma (MM) after 1–3 prior lines of therapy (LOT) in CARTITUDE-4[1,2]
- CARTITUDE-2 is a phase 2, multicohort study evaluating cilta-cel across various clinical settings of unmet need[3]
- CARTITUDE-2 cohort D is evaluating cilta-cel ± lenalidomide maintenance in patients with suboptimal response (did not achieve complete response [CR]) to frontline autologous stem cell transplant (ASCT), a population with historically poor outcomes[4–8]
  - Initial data with a median follow-up of 22.4 months demonstrated deep and durable responses[9]
  - Overall response rate (ORR) was 94.1%, minimal residual disease (MRD) negativity occurred in 80.0% of evaluable patients, and 18-month PFS and OS rates were 93.8% each[9]
- Here, we report updated efficacy and safety for this cohort with a median follow-up of 40.2 months

Methods

- The CARTITUDE-2 cohort D study design is shown in **Figure 1**
- Per protocol, safety was assessed in the first 5 patients who received cilta-cel only, without lenalidomide maintenance; subsequently, 12 patients initiated continuous lenalidomide maintenance ≥21 days post cilta-cel
- The primary endpoint was MRD negativity at 10^{-5} threshold using next-generation sequencing or next-generation flow
- Secondary endpoints included ORR (assessed per International Myeloma Working Group [IMWG] response criteria); duration of response (DOR), time to response; PFS and OS; incidence and severity of adverse events (AEs), including cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS), both of which were graded per American Society for Transplantation and Cellular Therapy criteria[10] (all other AEs were graded per Common Terminology Criteria for Adverse Events v5)

Figure 1: CARTITUDE-2 cohort D study design



[a]Bridging therapy was allowed when clinically indicated; alternative bridging regimens instead of, or in addition to, lenalidomide were allowed. [b]Per protocol, safety was assessed in the first 5 patients with cilta-cel only; subsequently, 12 patients initiated continuous lenalidomide maintenance starting as early as 21 days post cilta-cel for ≤2 years. Dose of 10 mg/day upon adequate hematologic recovery. Cy, cyclophosphamide; Flu, fludarabine.

Results

Baseline characteristics

- As of Feb 2025, 17 patients received cilta-cel, with a median follow-up of 40.2 months (range, 4.7–55.9; **Table 1**)

Table 1: Posttransplant baseline characteristics

Characteristic	N=17
Age, median (range), years	54.0 (37–69)
Male, n (%)	14 (82.4)
Race, n (%)	
White	14 (82.4)
Black	1 (5.9)
Not reported	2 (11.8)
ECOG PS at screening, n (%)	
0	13 (76.5)
1	4 (23.5)
Time from initial diagnosis to enrollment, median (range), years	0.9 (0.6–1.4)
Myeloma type by immunofixation, n (%)	
IgG	11 (64.7)
IgA	2 (11.8)
Light chain, kappa	2 (11.8)
Negative immunofixation	2 (11.8)
Extramedullary plasmacytomas, n (%)	0
High-risk cytogenetics,[a,b] n (%)	3 (17.6)
del(17p)	1 (5.9)
t(4;14)	2 (11.8)
ISS stage I, n (%)	17 (100)
Prior ASCT,[c] n (%)	17 (100)
Prior PI and IMiD, n (%)	17 (100)
Prior anti-CD38 mAb, n (%)	3 (17.6)

[a]Cytogenetic risk abnormalities based on central FISH testing, or local FISH testing and karyotype testing if central FISH not available; cytogenetic risk was assessed at time of enrollment, after induction and high-dose melphalan; high risk defined as having any of del(17p), t(4;14), t(14;16), t(14;20), or gain/amp(1q). [b]2 patients were unknown. [c]1 patient received tandem ASCT, ie, underwent ASCT twice. After ASCT, 9 patients had VGPR and 7 had PR; 1 patient who had tandem ASCT had VGPR after the first transplant, and status was not available after the second. ECOG PS, Eastern Cooperative Oncology Group performance status; Ig, immunoglobulin; IMiD, immunomodulatory drug; ISS, International Staging System; mAb, monoclonal antibody; PI, proteasome inhibitor; PR, partial response; VGPR, very good partial response.

Lenalidomide maintenance

- In 12 patients who initiated continuous lenalidomide maintenance after cilta-cel, lenalidomide was given at a dose of 10 mg daily upon adequate hematologic recovery (**Table 2**)
  - Lenalidomide maintenance was provided until confirmed progression, unacceptable toxicity, or 2 years after cilta-cel infusion (whichever occurred first)

Table 2: Lenalidomide maintenance

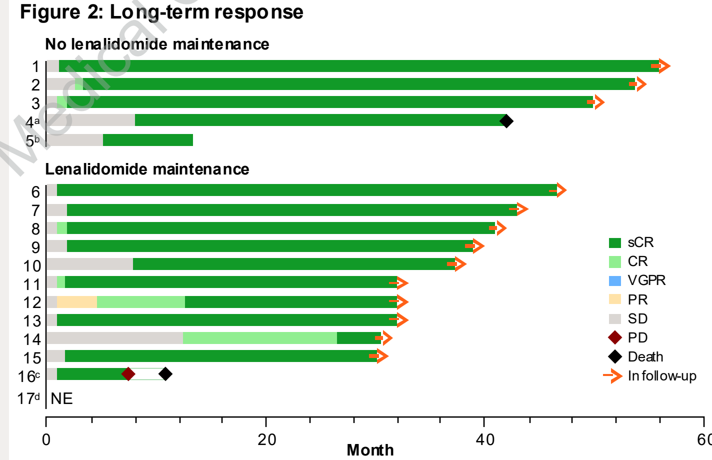
	Lenalidomide maintenance (n=12)
Time to initiation, median (range), days	51.0 (21.0–214.0)
Duration, median (range), days	696.5 (70.0–980.0)
Cycles, median (range)	24.5 (3.0–34.0)
Overall relative dose intensity,[a] median (range), %	93.4 (47.5–100)

[a]Relative dose intensity is calculated as the percentage of total dose (mg) received in all relevant cycles divided by the sum of prescribed doses (mg) in those cycles.

Response

- ORR (defined as the proportion of patients who achieved ≥PR per IMWG criteria) was achieved by 16/17 (94.1%) patients treated with cilta-cel; all of these patients had stringent CR (sCR)
- Responses to treatment with cilta-cel were durable (**Figure 2**); of the 16 responders:
  - 14 were alive and in ≥CR at last contact (follow-up range, 13.4–55.9 months), including 1 patient lost to follow-up on day 407
    - 1 progressed and died of MM at 11 months
    - 1 died in a motor vehicle accident while in response at 42 months

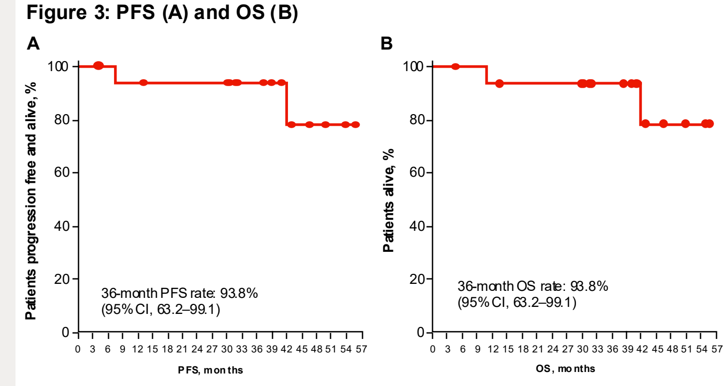
Figure 2: Long-term response



NE, not evaluable. [a]Died in motor vehicle accident while in response at 42 months. [b]Lost to follow-up on day 407. [c]Had disease progression and, at 11 months, died of MM. [d]NE for disease response and withdrew consent on day 142.

- PFS and OS rates were >90% at 3 years (**Figure 3**)

Figure 3: PFS (A) and OS (B)



- Of 16 MRD-evaluable patients, 13 (81.3%; [95% CI, 54.4–96.0]) achieved MRD negativity at 10^{-5} (**Table 3**)
- Median time to MRD negativity was 1.7 months (range, 0.9–11.5)

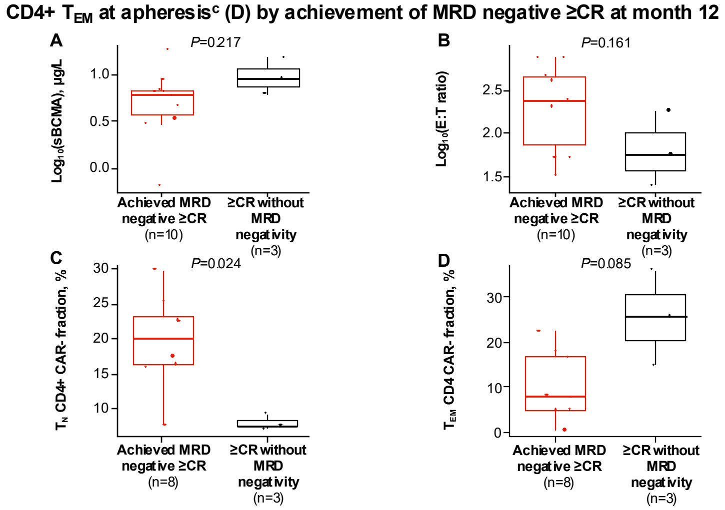
Table 3: MRD negativity

	MRD negativity
Overall	81.3% (13/16 evaluable patients[a])
	MRD-negative ≥CR rate[b]
12 months	71.4% (10/14 evaluable patients[c])
24 months	72.7% (8/11 evaluable patients[c])
36 months	75.0% (6/8 evaluable patients[c])

[a]Defined as having samples that passed calibration and quality control and had sufficient cells for testing at the 10^{-5} threshold. [b]Defined as the proportion of patients who were MRD negative by bone marrow aspirate at each time point (±3 months) and achieved ≥CR based on computerized algorithm, according to IMWG response criteria at each time point (+3 months). [c]Defined as having a positive, negative, or indeterminate MRD test within the time-point window (±3 months).

- Patients who achieved ≥CR with vs without MRD negativity exhibited a trend toward lower preinfusion soluble BCMA (sBCMA), higher effector-to-target (E:T) ratio, and enhanced baseline T-cell fitness reflected by a higher level of CD4+ naive T (T_N) and a lower level of CD4+ effector memory T (T_{EM}) (**Figure 4**)

Figure 4: Baseline sBCMA (A), E:T ratio[a] (B), CD4+ T_N at apheresis[b] (C), and CD4+ T_{EM} at apheresis[c] (D) by achievement of MRD negative ≥CR at month 12



[a]Defined as cilta-cel peak expansion over preinfusion sBCMA. [b]Consistent findings in CD8+ T_N. [c]Consistent findings in CD8+ T_{EM}.

Safety

- No new safety signals were observed at this longer follow-up
- 6 patients had CAR-T cell-related neurotoxicities (all previously reported)[9] and most events were transient and grade 1/2 except:
  - 1 patient with grade 3 diplopia (recovered before previous data cut-off)[9]
  - 1 patient with grade 1 paresthesia, which was ongoing from day 18 to time of withdrawal from study at 4.7 months post infusion
- There were no cases of parkinsonism or Guillain-Barré syndrome
- No new second primary malignancies were observed at this longer follow-up
  - 1 patient had grade 3 myelodysplastic syndrome (previously reported; ongoing at current data cut-off), with onset at day 353, and was not cilta-cel related per investigator assessment

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Multiple Myeloma

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