MM-567

Ciltacabtagene Autoleucel vs Standard of Care in Lenalidomide-Refractory Multiple Myeloma: Phase 3 CARTITUDE-4 Subgroup Analysis by Cytogenetic Risk

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Key Takeaway

Cilta-cel demonstrated consistent and robust efficacy regardless of cytogenetic risk status

Conclusions

Cilta-cel demonstrated favorable efficacy outcomes—including higher ORRs, higher rates of ≥CR and MRD negativity, and improved PFS—vs SOC in patients with high-risk cytogenetic abnormalities and standard-risk cytogenetics

The efficacy of cilta-cel vs SOC in CARTITUDE-4 supports cilta-cel as a potential new SOC in lenalidomide-refractory MM as early as first relapse, including in patients with high-risk cytogenetics

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Disclosures
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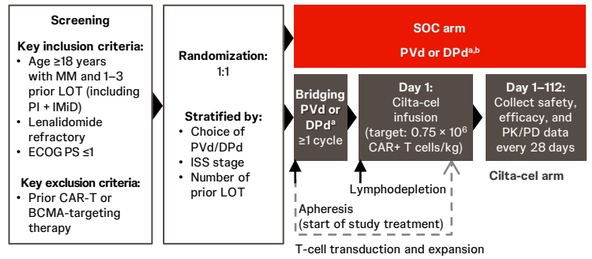
Introduction

- The phase 3 CARTITUDE-4 study is evaluating ciltacabtagene autoleucel (cilta-cel) vs standard of care (SOC) in patients with lenalidomide-refractory multiple myeloma (MM) and 1–3 prior lines of therapy (LOT)[1,2]
- In the primary analysis:
  - Cilta-cel prolonged progression-free survival (PFS; $P<0.0001$)[1]
  - Overall response rates (ORRs) were higher with cilta-cel vs SOC (85% vs 67%), as were rates of complete response (CR) or better (73% vs 22%)[1]
  - Minimal residual disease (MRD)-negativity rates were higher with cilta-cel vs SOC (61% vs 16%; 10^{-5} threshold)[1]
- Based on CARTITUDE-4 results, cilta-cel was recently approved in the US and the EU for patients with lenalidomide-refractory MM who have received ≥1 prior LOT[3,4]
- High-risk cytogenetic abnormalities in patients with lenalidomide-refractory MM negatively impact prognosis in real-world datasets (real-world PFS hazard ratio [HR], 1.39 [95% CI, 1.20–1.61] vs standard risk)[5]
  - However, some treatments may partially overcome the adverse effects of high-risk cytogenetics[6]
- We report the efficacy of cilta-cel compared with SOC in CARTITUDE-4 patients with high-risk cytogenetic abnormalities, including t(4;14), del(17p), t(14;16), and gain/amp(1q)

Methods

- CARTITUDE-4 is a randomized, open-label trial (**Figure 1**)
- Patients with high-risk cytogenetics had ≥1 of the following cytogenetic abnormalities at baseline determined by fluorescence in situ hybridization: t(4;14), del(17p), t(14;16), or gain/amp(1q)
- Due to low patient numbers, data for patients with t(14;16) are not shown as a separate subgroup but are included in the high-risk group

Figure 1: CARTITUDE-4 study design



[a]Physicians' choice. [b]Administered until disease progression.
BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; ISS, International Staging System; PD, pharmacodynamics; PI, proteasome inhibitor; PK, pharmacokinetics; PVd, daratumumab, bortezomib, and dexamethasone.

Results

Study population

- At data cut-off on November 1, 2022, the median follow-up was 15.9 (range, 0.1–27.3) months
- Of 419 randomized patients, 394 were evaluable, 255 had high-risk cytogenetics, and 139 had standard-risk cytogenetics (**Table 1**)
- Baseline characteristics were similar in patients with high-risk cytogenetics in the cilta-cel vs SOC arms

Table 1: Baseline characteristics in patients with high-risk cytogenetics

Characteristic	High risk	
	Cilta-cel (n=123)	SOC (n=132)
Age, median (range), years	62 (40–78)	62 (35–80)
Male	65 (52.8)	71 (53.8)
Cytogenetic high-risk abnormality		
gain/amp(1q)	**89 (72.4)**	**107 (81.1)**
del(17p)	**49 (39.8)**	**43 (32.6)**
t(4;14)	**30 (24.4)**	**30 (22.7)**
t(14;16)	**3 (2.4)**	**7 (5.3)**
≥2 high-risk abnormalities	**43 (35.0)**	**49 (37.1)**
del(17p), t(14;16), or t(4;14)	**73 (59.3)**	**69 (52.3)**
ISS stage		
I	77 (62.6)	79 (59.8)
II	38 (30.9)	46 (34.8)
III	8 (6.5)	7 (5.3)
Soft tissue plasmacytomas	27 (22.0)	20 (15.2)
Years since diagnosis, median (range)	3.2 (0.5–12.1)	3.4 (0.5–13.2)
Prior LOT, median (range)		
1	39 (31.7)	45 (34.1)
2–3	84 (68.3)	87 (65.9)
Previous ASCT	104 (84.6)	120 (90.9)
Triple-class exposed[a]	33 (26.8)	34 (25.8)
Refractory status		
Daratumumab	29 (23.6)	27 (20.5)
Triple-class[a]	17 (13.8)	20 (15.2)
To last LOT	121 (98.4)	130 (98.5)
Bridging therapy		
DPd	106 (86.2)	116 (87.9)
PVd	17 (13.8)	16 (12.1)

All data are n (%) unless otherwise specified.
[a]Includes ≥1 PI, ≥1 IMiD, and 1 anti-CD38 monoclonal antibody.
ASCT, autologous stem cell transplant.

Efficacy

- Overall, high-risk cytogenetics were not associated with poorer outcomes with cilta-cel; by contrast, efficacy in the SOC arm was lower in patients with high-risk cytogenetics than in those with standard-risk cytogenetics (**Table 2**)

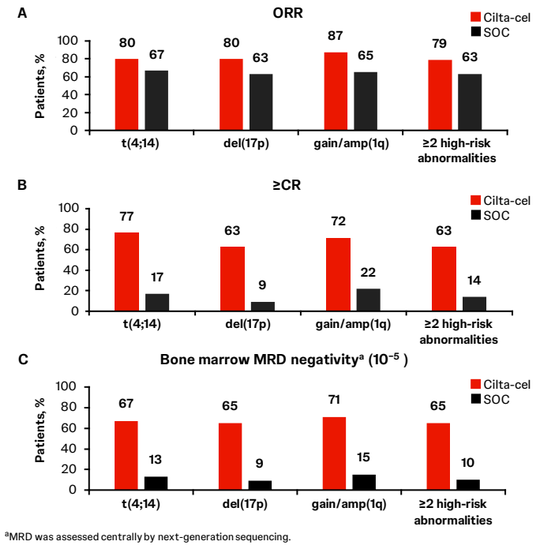
Table 2: Efficacy outcomes by cytogenetic risk

Endpoint	Cilta-cel		SOC	
	Standard risk (n=69)	High risk (n=123)	Standard risk (n=70)	High risk (n=132)
ORR, n (%)	59 (85.5)	105 (85.4)	50 (71.4)	87 (65.9)
≥CR, n (%)	51 (73.9)	90 (73.2)	18 (25.7)	26 (19.7)
MRD negativity (10^{-5}), n (%)	34 (49.3)	86 (69.9)	13 (18.6)	19 (14.4)
PFS, median (95% CI), mo	NE (NE–NE)	NE (18.4–NE)	20.6 (11.2–NE)	10.3 (7.6–12.5)

NE, not evaluable.

- The ORR was higher, and the rates of ≥CR and bone marrow MRD negativity were substantially higher with cilta-cel than with SOC for each abnormality (**Figure 2**)

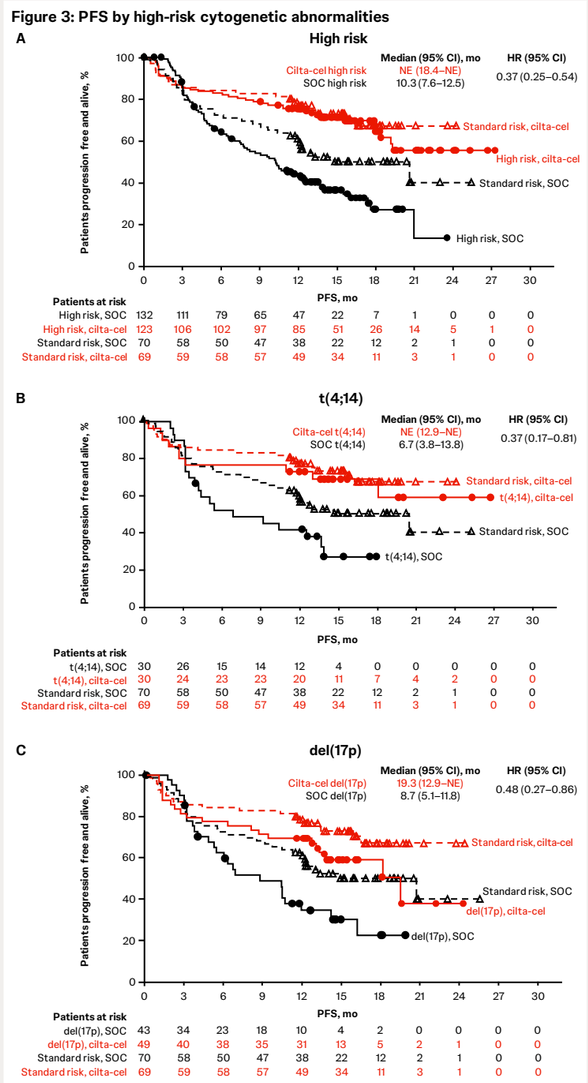
Figure 2: Treatment response by cytogenetic risk abnormality



[a]MRD was assessed centrally by next-generation sequencing.

- Cilta-cel lessens the impact of high-risk cytogenetics on PFS and also improved PFS vs SOC (**Figure 3A**)
  - In patients with gain/amp(1q), the median PFS was NE with cilta-cel (95% CI, 18.4–NE) vs 10.3 (95% CI, 7.5–14.0) months with SOC (HR, 0.37 [95% CI, 0.24–0.59])
  - The median PFS rates for t(4;14) and del(17p) are shown in **Figures 3B** and **3C**

Figure 3: PFS by high-risk cytogenetic abnormalities



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Multiple Myeloma

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