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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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Poster

https://www.congresshub.com/Oncology/EHA2024/Cilta-cel/Mina

Acknowledgments
This study was funded by Janssen Research & Development, LLC and Legend Biotech USA Inc. Medical writing support was provided by Rebekah Dedrick, PhD, of Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC.

Disclosures
RM has received fees for consulting, advisory committees, and/or honoraria from Amgen, BMS, Celgene, Janssen, Pfizer, Sanofi, and Takeda.

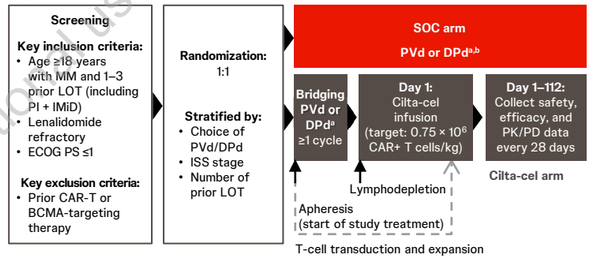
Introduction

- 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**)

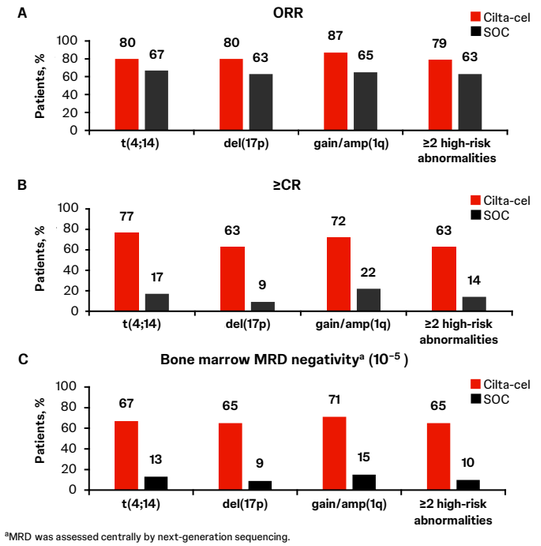
Table 2: Efficacy outcomes by cytogenetic risk

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**)

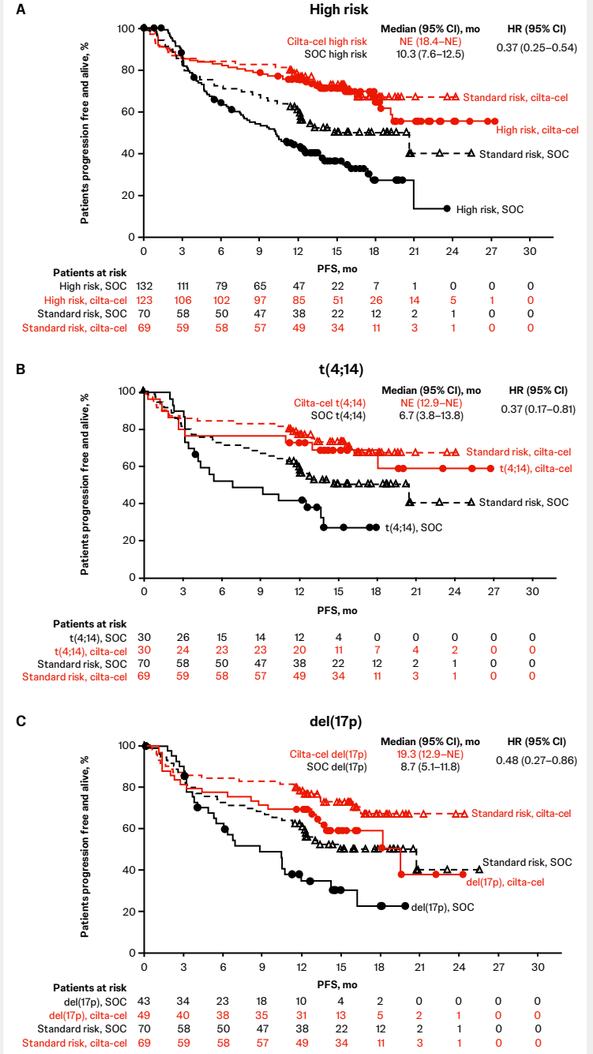
Figure 2: Treatment response by cytogenetic risk abnormality



[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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Presented by R Mina at the European Hematology Association (EHA) 2024 Hybrid Congress; June 13–16, 2024; Madrid, Spain