MM-1070

Ciltacabtagene Autoleucel (Cilta-cel) vs Standard of Care (SOC) in Patients (Pts) with Relapsed/Refractory Multiple Myeloma (MM): CARTITUDE-4 Survival Subgroup Analyses

Surbhi Sidana[1] (surbhi.sidana@stanford.edu), Joaquín Martínez-López[2], Abdullah M Khan[3], Albert Oriol[4], Andrew Spencer[5], Binod Dhakal[6], Yaël C Cohen[7], Cyrille Touzeau[8-10], Dominik Dytfeld[11], Hermann Einsele[12], Jesús San-Miguel[13], Salomon Manier[14], Diana Chen[15], Katherine Li[16], Nina Benachour[17], Carolina Lonardi[18], Arnab Ghosh[19], Nitin Patel[20], Erika Florendo[20], Simon J Harrison[21-23]

[1]Stanford University School of Medicine, Stanford, CA, USA; [2]Hospital 12 de Octubre, Complutense University CNIO, MIC, Madrid, Spain; [3]The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [4]Institut Català d'Oncologia and Institut Josep Carreras, Hospital Germans Trias i Pujol, Badalona, Barcelona, Spain; [5]Alfred Health-Monash University, Melbourne, VIC, Australia; [6]Medical College of Wisconsin, Milwaukee, WI, USA; [7]Tel Aviv Sourasky (Ichilov) Medical Center, Faculty of Medical & Health Sciences, Tel Aviv University, Tel Aviv, Israel; [8]Service d'hématologie, Centre Hospitalier Universitaire (CHU) Hotel Dieu, Nantes, France; [9]Centre de Recherche en Cancérologieet Immunologie Intégrée Nantes Angers, INSERM, Centre National de la Recherche Scientifique, Université d'Angers, Université de Nantes, France; [10]Site de Recherche Intégrée sur le Cancer, Imaging and Longitudinal Investigations to Ameliorate Decision-making (ILIAD), French National Cancer Institute–French Ministry of Health–INSERM 12558, Nantes, France; [11]Poznan University of Medical Sciences, Poznań, Poland; [12]Universitätsklinikum Würzburg, Medizinische Klinik und Poliklinik II, Würzburg, Germany; [13]Cancer Center Clinica Universidad de Navarra, CIMA, IDISNA, Pamplona, Spain; [14]University of Lille, CHU Lille, Lille, France; [15]Johnson & Johnson, Shanghai, China; [16]Johnson & Johnson, Spring House, PA, USA; [17]Johnson & Johnson, Beerse, Belgium; [18]Johnson & Johnson, Buenos Aires, Argentina; [19]Johnson & Johnson, Raritan, NJ, USA; [20]Legend Biotech USA Inc., Somerset, NJ, USA; [21]Peter MacCallum Cancer Centre, Melbourne, VIC, Australia, and Royal Melbourne Hospital, Melbourne, VIC, Australia; [22]Translation Laboratory, Centre of Excellence in Cellular Immunotherapy, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [23]Sir Peter MacCallum Department of Oncology, University of Melbourne, Parkville, VIC, Australia

Key Takeaway

Cilta-cel improved PFS and OS vs SOC across subgroups in CARTITUDE-4, including patients with standard- and high-risk cytogenetics, EMD, and 1 pLOT and beyond

Conclusions

ITT analysis showed that cilta-cel improved PFS and OS vs SOC across subgroups, including patients with EMD and 1 pLOT and beyond

Compared with SOC, cilta-cel improved PFS and OS in patients with high-risk cytogenetics, suggesting it may overcome the poor prognosis associated with these high-risk features

These data continue to support a positive benefit-risk ratio for cilta-cel in patients with lenalidomide-refractory MM as early as after first relapse

Introduction

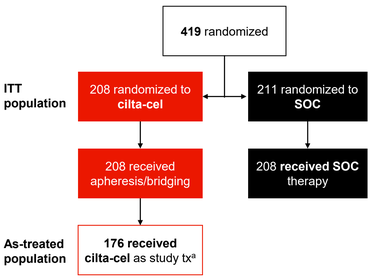
- In CARTITUDE-4 (NCT04181827), a single cilta-cel infusion significantly prolonged progression-free survival (PFS) and overall survival (OS) in patients with lenalidomide-refractory MM after 1–3 prior lines of therapy (pLOT)[1]
  - At median follow up of 33.6 months, PFS (hazard ratio [HR] weighted, 0.29 [95% CI, 0.22–0.39]) and OS (HR, 0.55 [0.39–0.79]; *P*=0.0009) were significantly improved vs SOC[1]
  - Overall minimal residual disease (MRD)-negative complete response (CR) or better rates (82.1% vs 25.2%) as well as sustained (≥12 months) MRD-negative ≥CR (51.7% vs 9.7%) rates in evaluable patients were higher in the cilta-cel arm vs SOC[2]
- Here, we report PFS and OS from subgroups of patients with standard-/high-risk cytogenetics, with/without extramedullary disease (EMD), and with 1, 2, or 3 pLOT

Methods

Treatment and data analysis

- CARTITUDE-4 study design has been described previously[3]
- Patients (n=208) randomized to the cilta-cel arm underwent apheresis, bridging treatment, lymphodepletion, and then a single cilta-cel infusion (n=176; **Figure 1**)
- Bridging treatment consisted of either:
  - Pomalidomide, bortezomib, and dexamethasone (PVd) or
  - Daratumumab, pomalidomide, and dexamethasone (DPd)

Figure 1: Randomization and treatment



[a]32 patients did not receive cilta-cel as study treatment (n=30 due to disease progression; n=2 due to death during bridging therapy/lymphodepletion), of which 20 received cilta-cel as subsequent LOT. ITT, intent to treat; LOT, line of therapy; tx, treatment.

- Patients (n=211) randomized to the SOC arm received physician's choice of PVd or DPd until disease progression (n=208)
- PFS was assessed using a validated computerized algorithm; HR was analyzed using unweighted Cox proportional hazards model for the ITT analysis set

Acknowledgments

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Disclosures

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Results

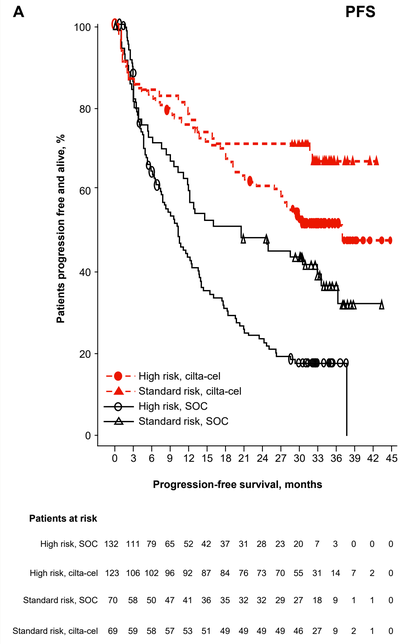
Study population

- As of May 1, 2024, the median follow-up was 33.6 months (range, 0.1–45.0)

Cilta-cel vs SOC by cytogenetic risk

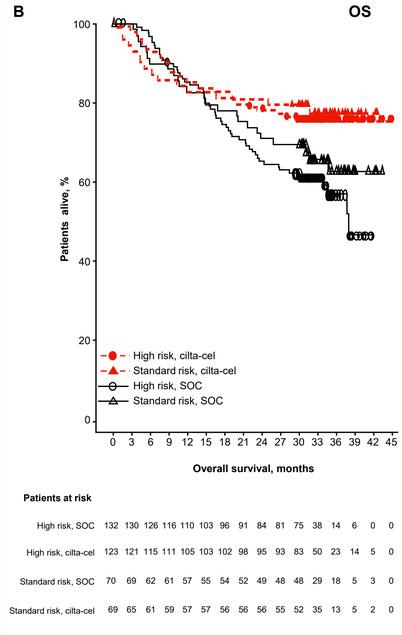
- Cilta-cel consistently improved PFS and OS compared with SOC in patients with standard risk and high risk (**Figures 2** and **3**)
  - High-risk cytogenetics was defined as del(17p), t(4;14), t(14;16), or gain/amp(1q) by fluorescence in situ hybridization

Figure 2: Kaplan-Meier analysis of patients with standard-risk and high-risk cytogenetics



Patients at risk

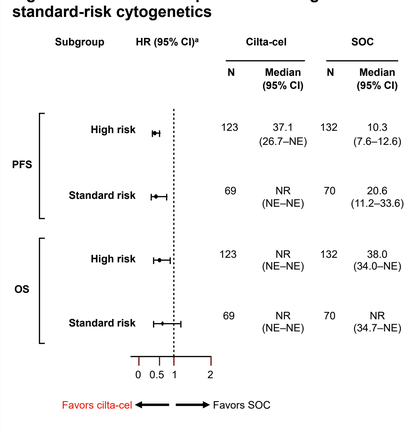
High risk, SOC	132	111	79	65	52	42	37	31	28	23	20	7	3	0	0	0
High risk, cilta-cel	123	106	102	96	92	87	84	76	73	70	55	31	14	7	2	0
Standard risk, SOC	70	58	50	47	41	36	35	32	32	29	27	18	9	1	1	0
Standard risk, cilta-cel	69	59	58	57	53	51	49	49	49	49	46	27	9	2	1	0



Patients at risk

High risk, SOC	132	130	126	116	110	103	96	91	84	81	75	38	14	6	0	0
High risk, cilta-cel	123	121	115	111	105	103	102	98	95	93	83	50	23	14	5	0
Standard risk, SOC	70	69	62	61	57	55	54	52	49	48	48	29	18	5	3	0
Standard risk, cilta-cel	69	65	61	59	57	57	56	56	56	55	52	35	13	5	2	0

Figure 3: PFS and OS in patients with high-risk and standard-risk cytogenetics

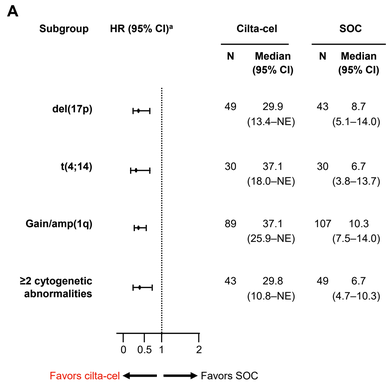


ITT population, median PFS and OS are shown in months. PFS was estimated by the Kaplan-Meier method. [a]Hazard ratio and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable. NE, not estimable; NR, not reached.

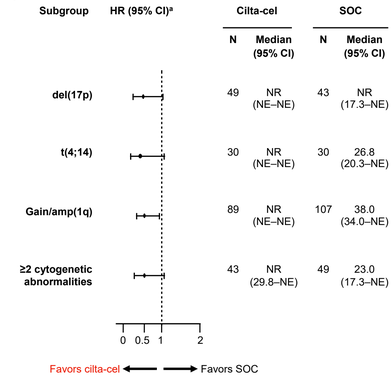
- Cilta-cel improved PFS and OS compared with SOC in patients with del(17p), t(4;14), gain/amp(1q), and ≥2 cytogenetic abnormalities from the ITT population (**Figure 4**)

Figure 4: (A) PFS and (B) OS in cytogenetic high-risk MM

A



B

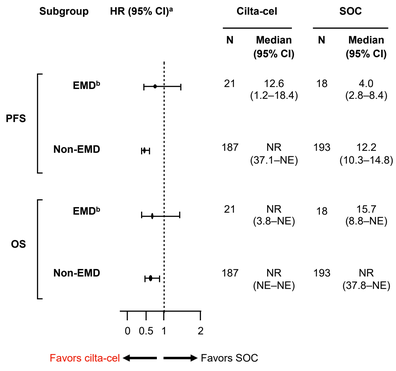


Median PFS and OS are shown in months. PFS was estimated by the Kaplan-Meier method. [a]Hazard ratio and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable. The subgroup (n=7) size for t(14;16) was too small to derive reliable statistics.

Cilta-cel for patients with EMD

- Cilta-cel improved median PFS and OS compared with SOC in patients with EMD (**Figure 5**)
- Of 21 patients with EMD randomized to cilta-cel, 13 received cilta-cel as study treatment
  - In the as-treated population with EMD (N=13), median PFS (95% CI) was 18.4 (12.6–NE) and median OS (95% CI) was NR (NE–NE)

Figure 5: PFS and OS in patients with EMD and non-EMD

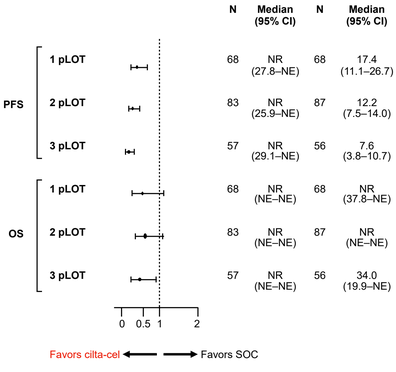


ITT population, median PFS and OS are shown in months. PFS was estimated by the Kaplan-Meier method. [a]Hazard ratio and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable. [b]Extramedullary disease denotes soft tissue plasmacytoma that was not contiguous with bone.

Cilta-cel for patients with 1–3 pLOT

- Cilta-cel significantly improved PFS and OS compared with SOC in patients with MM in each subgroup of pLOT (**Figure 6**)

Figure 6: PFS and OS in patients with pLOT



ITT population, median PFS and OS are shown in months. PFS was estimated by the Kaplan-Meier method. [a]Hazard ratio and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable.

References

1. Mateos M-V, et al. *Clin Lymphoma Myeloma Leuk.* 2024;24(suppl 2):S290. **2.** Popat R, et al. *Blood.* 2024;144(suppl 1):1032. **3.** San-Miguel J, et al. *N Engl J Med.* 2023;389:335-47.