PS1723

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

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Key Takeaway

Cilta-cel improved PFS and OS vs SOC across subgroups in CARTITUDE-4, including pts 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 pts with EMD and 1 pLOT and beyond
- Compared with SOC, cilta-cel improved PFS and OS in pts 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 pts with lenalidomide-refractory MM as early as after first relapse

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Disclosures

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Introduction

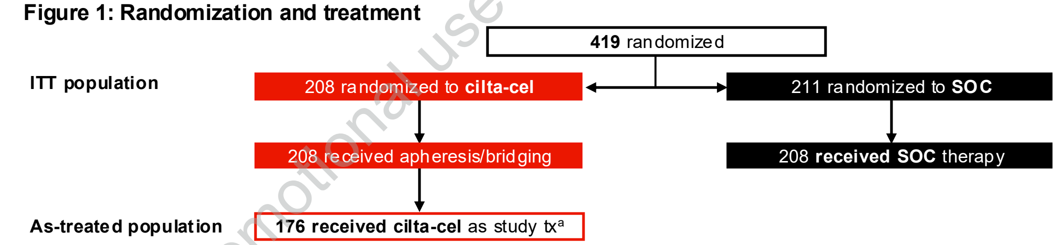
- In CARTITUDE-4 (NCT04181827), a single cilta-cel infusion significantly prolonged progression-free survival (PFS) and overall survival (OS) in pts with lenalidomide-refractory MM after 1–3 prior lines of therapy (pLOT)[1]
  - At median follow-up of 33.6 months, PFS (hazard ratio [HR] weighted, 0.29 [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 pts were higher in the cilta-cel arm vs SOC[2]
- Here, we report PFS and OS from subgroups of pts 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]
- Pts (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 pts 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.

- Pts (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 an unweighted Cox proportional hazards model for the ITT analysis set

Results

Study population

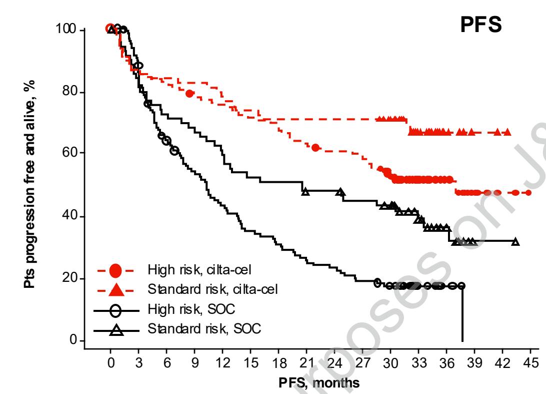
- As of May 1, 2024, the median follow-up was 33.6 months (range, 0.1–45.0)

Cilta-cel vs SOC by cytogenetic risk

- Cilta-cel consistently improved PFS and OS compared with SOC in pts 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

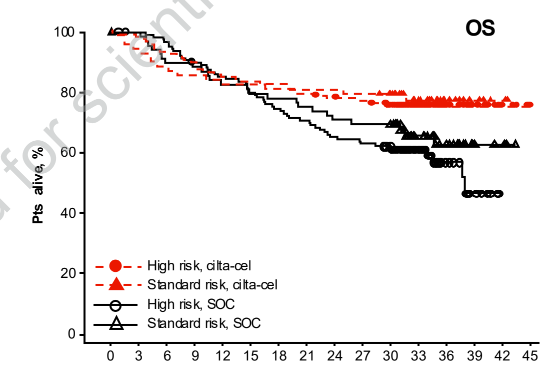
Figure 2: Kaplan-Meier analysis of pts with standard- and high-risk cytogenetics

A



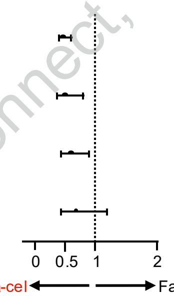
Pts at risk																
High risk, SOC	132	111	79	65	52	42	37	31	28	23	20	7	3	0	0	0
High risk, cilta-cel	123	106	102	96	92	87	84	76	73	70	55	31	14	7	2	0
Standard risk, SOC	70	58	50	47	41	36	35	32	32	29	27	18	9	1	1	0
Standard risk, cilta-cel	69	59	58	57	53	51	49	49	49	49	46	27	9	2	1	0

B



Pts 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 pts with high- and standard-risk cytogenetics



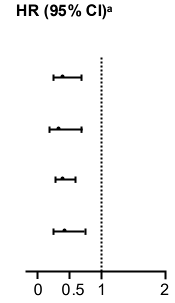
	Subgroup	Cilta-cel N	Cilta-cel Median (95% CI)	SOC N	SOC Median (95% CI)
PFS	High risk	123	37.1 (26.7–NE)	132	10.3 (7.6–12.6)
	Standard risk	69	NR (NE–NE)	70	20.6 (11.2–33.6)
OS	High risk	123	NR (NE–NE)	132	38.0 (34.0–NE)
	Standard risk	69	NR (NE–NE)	70	NR (34.7–NE)

ITT population, median PFS and OS are shown in months. PFS was estimated by the Kaplan-Meier method.
[a]HR 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 pts with del(17p), t(4;14), gain/amp(1q), and ≥2 cytogenetic abnormalities from the ITT population (**Figure 4**)

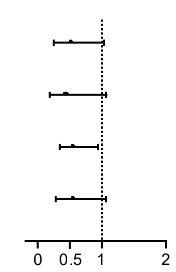
Figure 4: (A) PFS and (B) OS in cytogenetic high-risk MM

A



Subgroup	Cilta-cel N	Cilta-cel Median (95% CI)	SOC N	SOC Median (95% CI)
del(17p)	49	29.9 (13.4–NE)	43	8.7 (5.1–14.0)
t(4;14)	30	37.1 (18.0–NE)	30	6.7 (3.8–13.7)
Gain/amp(1q)	89	37.1 (25.9–NE)	107	10.3 (7.5–14.0)
≥2 cytogenetic abnormalities	43	29.8 (10.8–NE)	49	6.7 (4.7–10.3)

B



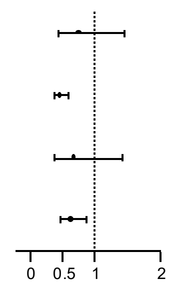
Subgroup	Cilta-cel N	Cilta-cel Median (95% CI)	SOC N	SOC Median (95% CI)
del(17p)	49	NR (NE–NE)	43	NR (17.3–NE)
t(4;14)	30	NR (NE–NE)	30	26.8 (20.3–NE)
Gain/amp(1q)	89	NR (NE–NE)	107	38.0 (34.0–NE)
≥2 cytogenetic abnormalities	43	NR (29.8–NE)	49	23.0 (17.3–NE)

Median PFS and OS are shown in months. PFS was estimated by the Kaplan-Meier method. [a]HR 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 pts with EMD

- Cilta-cel improved median PFS and OS compared with SOC in pts with EMD (**Figure 5**)
- Of 21 pts 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 pts with EMD and non-EMD



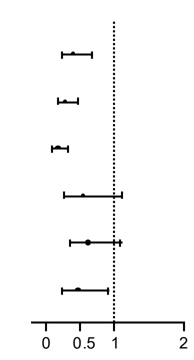
	Subgroup	Cilta-cel N	Cilta-cel Median (95% CI)	SOC N	SOC Median (95% CI)
PFS	EMD[b]	21	12.6 (1.2–18.4)	18	4.0 (2.8–8.4)
	Non-EMD	187	NR (37.1–NE)	193	12.2 (10.3–14.8)
OS	EMD[b]	21	NR (3.8–NE)	18	15.7 (8.8–NE)
	Non-EMD	187	NR (NE–NE)	193	NR (37.8–NE)

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

Cilta-cel for pts with 1–3 pLOT

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

Figure 6: PFS and OS in pts with pLOT



	Subgroup	Cilta-cel N	Cilta-cel Median (95% CI)	SOC N	SOC Median (95% CI)
PFS	1 pLOT	68	NR (27.8–NE)	68	17.4 (11.1–26.7)
	2 pLOT	83	NR (25.9–NE)	87	12.2 (7.5–14.0)
	3 pLOT	57	NR (29.1–NE)	56	7.6 (3.8–10.7)
OS	1 pLOT	68	NR (NE–NE)	68	NR (37.8–NE)
	2 pLOT	83	NR (NE–NE)	87	NR (NE–NE)
	3 pLOT	57	NR (NE–NE)	56	34.0 (19.9–NE)

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

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Multiple Myeloma