P-057

Comparative Efficacy of Cilta-Cel vs Approved Comparator Treatments for Patients With Relapsed/Refractory Multiple Myeloma With 1-3 Prior Lines of Therapy: A Network Meta-Analysis

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Key Takeaways

Results of the NMA showed statistically significant PFS benefit for cilta-cel compared to all comparator regimens analyzed (Pd, IsaPd, EloPd, Md).

Limited subgroup results were reported across the included trials; with only LEN-refractory patients and those that had previously received 2 or 3 prior LOT being commonly reported for the outcome of interest. The NMA results were consistent across analyses performed based on the ITT populations, LEN-refractory subgroups, and 2-3 prior LOT subgroups.

Differences between patients in CARTITUDE-4 and APOLLO with regards to prior exposure to anti-CD38 must be considered in the context of the NMA findings; CARTITUDE-4 patients were exposed to prior daratumumab (25%), while patients in APOLLO were not (0%). This difference likely resulted in estimates of PFS that were conservative for cilta-cel, given that APOLLO was required to link cilta-cel to the network.

Conclusions

These comparisons provide valuable information to contextualize the efficacy of cilta-cel in patients who are LEN refractory and have received 1–3 prior lines and of therapy in whom SOC may be different from DPd or PVd.

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Poster

https://www.congresshub.com/Oncology/IMS2024/Cilta-cel/Mina

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Disclosures

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Background

- The efficacy and safety of cilta-cel versus standard-of-care (SOC) treatments (daratumumab, pomalidomide, and dexamethasone [DPd] or pomalidomide, bortezomib, and dexamethasone [PVd]) was demonstrated in the phase 3 CARTITUDE-4 trial,[1] (NCT04181827) in RRMM patients who received 1–3 prior line(s) of therapy (LOT) that included an immunomodulatory agent (IMiD) and a proteasome inhibitor (PI), and who are refractory to lenalidomide (LEN).
- Other therapies considered to be SOC beyond DPd and PVd for patients with 1–3 prior LOT who are LEN-refractory include: daratumumab + bortezomib + dexamethasone (DVd), daratumumab + carfilzomib + dexamethasone (DKd), isatuximab + carfilzomib + dexamethasone (IsaKd), selinexor + bortezomib + dexamethasone (SVd), elotuzumab + pomalidomide + dexamethasone (EloPd), and isatuximab + pomalidomide + dexamethasone (IsaPd).

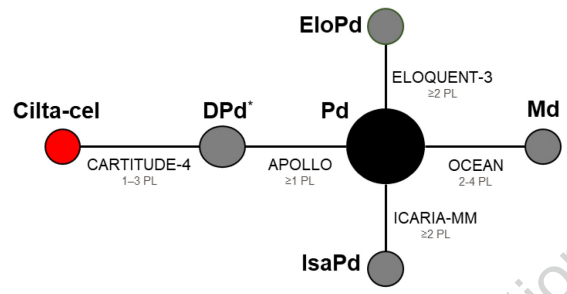
Objectives

- The objective of this analysis was to estimate the relative efficacy of cilta-cel versus SOC comparators that were not assessed in CARTITUDE-4 via network meta-analysis (NMA).

Methods

- A systematic literature review identified 22 randomized controlled trials (RCTs) assessing relevant comparator regimens of interest.
- The feasibility of NMA was assessed by determining 1) network connectivity (i.e. presence of a common comparator), 2) the degree of overlap with the CARTITUDE-4 population in terms of potential effect modifiers (including but not limited to the number of prior LOTs, LEN-refractoriness, and cytogenetic risk), and 3) the availability of common outcomes in terms of definition, assessor, and data maturity.
- DPd was the most frequently utilized treatment in the SOC arm of CARTITUDE-4 (representing 87% of patients) and almost identical results were observed for the DPd cohort and ITT population (HRs for PFS [95%CI]: 0.26 [0.18, 0.38] and 0.26 [0.18, 0.39], respectively). Given this, an assumption was made that the SOC arm in CARTITUDE-4 was comparable to the DPd arm in APOLLO to form a network of trials (Figure 1).

FIGURE 1: Network of Trials Included in NMA



* 87% of patients in CARTITUDE-4 received DPd and 13% received PVd
Cilta-cel = ciltacabtagene autoleucel; DPd = daratumumab, pomalidomide, and dexamethasone; EloPd = elotuzumab + pomalidomide + dexamethasone; IsaPd = isatuximab + pomalidomide + dexamethasone; Md = melflufen + dexamethasone; Pd = pomalidomide; PL = prior lines of therapy

- The network was centralized around pomalidomide in combination with dexamethasone (Pd) and included: CARTITUDE-4 (cilta-cel),[1] APOLLO (DPd and Pd),[2] ELOQUENT-3 (EloPd),[3] ICARIA-MM (IsaPd),[4] and OCEAN (melflufen, dexamethasone (Md).[5]
- There was no way to link the Pd-centralized network to DVd, DKd, IsaKd, SVd and therefore, alternative ITC methods were considered for these comparators.
- Fixed effects Bayesian NMAs were conducted to estimate hazard ratios (HR) for independent review committee (IRC) assessed progression-free survival (PFS), and 95% credible intervals (CrI) including all identified studies. It was assumed that PFS assessed by computerized algorithm in CARTITUDE-4 and APOLLO was comparable to IRC assessed PFS in the other trials.
- Primary PFS results from CARTITUDE-4 were analyzed using constant piecewise weighted (CPW) log-rank test methods; whereas a sensitivity analysis was based on 'unweighted' log-rank test methods. Given this, analyses were performed using results from CARTITUDE-4 based on both approaches, with the standard 'unweighted' results being considered the base case.
- Given differences across the ITT populations in the trials, NMA analyses were performed for the ITT populations and additionally, LEN-refractory patients, and those with 2-3 prior LOT, utilizing subgroup data where required.

Results

- The baseline characteristics of trials included in the NMA are presented in **Table 1**.
- Data inputs used in the NMA analyses are presented in **Table 2**.
- Since CARTITUDE-4 was conducted in a LEN-refractory population, analyses performed using LEN-refractory subgroup from comparator trials included the ITT data from CARTITUDE-4. Similarly, OCEAN was conducted in >99% LEN-refractory patients who had received 2-4 prior LOT, and given the lack of subgroup results available from this trial, subgroup analyses were performed using ITT data from OCEAN and subgroup data from the comparator trials.
- Subgroup results for LEN-refractory patients was not reported for ELOQUENT-3.

TABLE 1: Summary of Baseline Characteristics for Trials Included in NMA

Trial	Median Prior LOT (range)	Prior LOT	Prior Therapy	Refractory Status	Median Age (range)	ECOG PS	ISS Stage	Cytogenetic Risk	EMD (Yes)
CARTITUDE-4	2 (1–3)	1: 32% 2: 41% 3: 27%	LEN: 100% PI: 100% BOR: 97% K: 34% IXA: 10%	LEN: 100% PI: 48% Anti-CD38: 23%	61 (27–80)	0: 56% 1: 43% 2: 1%	I: 64% II: 30% III: 6%	High: 61% Standard: 33% Missing: 6%	18.9%
APOLLO	2 (1–5)	1: 11% 2-3: 75% ≥4: 14%	LEN: 100% PI: 100% BOR: 96% K: 27% IXA: 11%	LEN: 80% PI: 48% PI +IMiD: 42%	67 (35–90)	0: 55% 1: 37% 2: 8%	I: 45% II: 33% III: 22%	High: 24% Standard: 45% Missing: 31%	8%
ELOQUENT-3	3 (2–8)	2-3: 61% ≥4: 39%	LEN: 99% BOR: 100% K: 21% IXA: 6%	LEN: 87% PI: 80% LEN + PI: 70%	68 (36–81)	NR	I/II: 88% III: 12%	High: 24% Standard: 49% Missing: 27%	NR
ICARIA-MM	3 (2–4)	2-3: 66% ≥4: 34%	LEN: 100% PI: 100%	LEN: 93% PI: 76% LEN + PI: 71% IMiD: 95%	67 (59–74*)	NR	I: 38% II: 36% III: 26%	High risk: 20% Standard risk: 59% Missing: 21%	8%**
OCEAN	3 (2–4)	2: 45% 3-4: 55%	LEN: >99% PI: 65%	LEN: >99%	68 (60–72*)	0: 37% 1: 54% 2: 9%	I: 49% II: 38% III: 13%	High risk: 35% Standard risk: 52%	12%

*Interquartile range
** Patients with extramedullary/extraosseous and paraskeletal soft-tissue plasmacytomas
BOR = bortezomib; DARA: daratumumab; ECOG = Eastern Cooperative Oncology Group; EMD = extramedullary disease; ISS = International Stating System; LEN = lenalidomide; LOT = line of therapy; NR = not reported; PI = proteasome inhibitor; PS = performance status

TABLE 2: Data Inputs Used for NMA of Progression-Free Survival

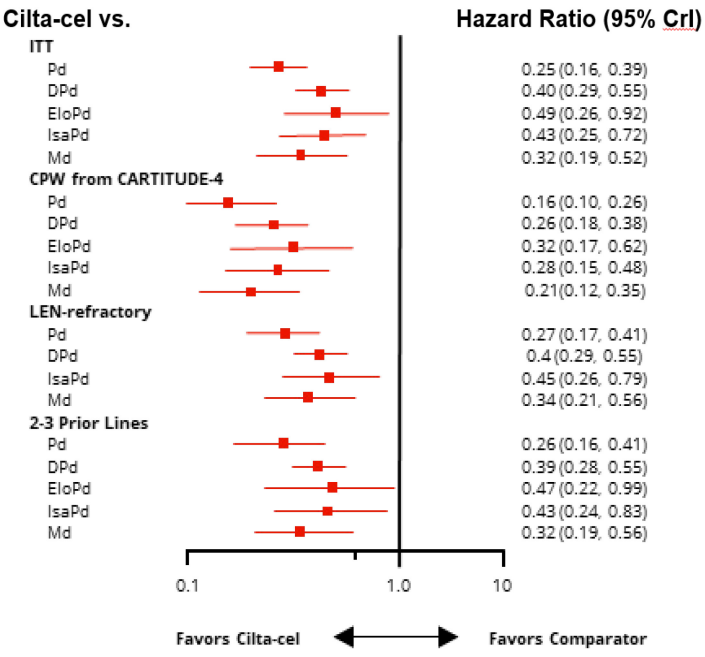
Trial Name	Data cut (Median f/u, months)	Analysis Population	N	HR (95%CI)
CARTITUDE-4 Cilta-cel vs. SOC	November 2022 (16.0)	ITT – 'unweighted'	419	0.40 (0.29, 0.55)
		ITT - CPW		0.26 (0.18, 0.38)
		2-3 PL - 'unweighted'	283	0.39 (0.28, 0.56)
		2-3 PL - CPW	283	0.24 (0.16, 0.37)
APOLLO DPd vs. Pd	July 2020 (17.5 vs. 16.4)	ITT	304	0.63 (0.47, 0.85)
		LEN refractory	242	0.66 (0.49, 0.90)
		2-3 PL	144	0.66 (0.48, 0.92)
ELOQUENT-3 EloPd vs. Pd	February 2018 (minimum 9.1)	ITT	117	0.51 (0.32, 0.82)
		LEN refractory	NA	NR
		2-3 PL	72	0.55 (0.31, 0.98)
ICARIA-MM IsaPd vs. Pd	October 2018 (11.6)	ITT	307	0.60 (0.46, 0.78)
		LEN refractory	284	0.59 (0.43, 0.82)
		2-3 PL	203	0.59 (0.40-0.90)
OCEAN Md vs. Pd	February 2021 (15.5 vs. 16.3)	ITT	495	0.79 (0.64, 0.98)
		LEN refractory	430	0.79 (0.64, 0.98)*
		2-3 PL	NA	0.79 (0.64, 0.98)*

*ITT population results were included in the subgroup analyses for LEN-refractory and 2-3 PL
Cilta-cel = ciltacabtagene autoleucel; CPW = constant piecewise weighted; CrI = credible interval; DPd = EloPd = elotuzumab, pomalidomide, dexamethasone; HR = hazard ratio; IsaPd = isatuximab, pomalidomide, dexamethasone; ITT = intention to treat; LEN = lenalidomide; Md = melflufen + dexamethasone; Pd= pomalidomide, dexamethasone; PL = prior line; SOC = standard of care

NMA Result for Progression-Free Survival

- The NMA found cilta-cel to be associated with a statistically significant PFS benefit versus all comparators of interest and across all populations analyzed (**Figure 2**). Results of analyses utilizing the CPW data from the CARTITUDE-4 showed the greatest PFS benefit for cilta-cel versus comparators.
- Consistent results were observed across the full ITT populations, LEN-refractory subgroups, and 2-3 prior LOT subgroups.

FIGURE 2: Progression-Free Survival NMA Results for Cilta-cel vs. Comparator Treatments



Cilta-cel = ciltacabtagene autoleucel; CPW = constant piecewise weighted; CrI = credible interval; DPd = EloPd = elotuzumab, pomalidomide, dexamethasone; IsaPd = isatuximab, pomalidomide, dexamethasone; LEN = lenalidomide; Md = melflufen + dexamethasone; NMA = network meta-analysis; Pd= pomalidomide, dexamethasone; SOC = standard of care

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