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Comparative Efficacy of Ciltacabtagene Autoleucel (Cilta-cel) Versus Belantamab Mafodotin (Belamaf), Bortezomib, and Dexamethasone and Versus Belamaf, Pomalidomide, and Dexamethasone in Patients With Relapsed/Refractory Multiple Myeloma (RRMM) Previously Treated With 1–3 Prior Lines of Therapy Using a Matching-Adjusted Indirect Comparison

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Key Takeaway

Indirect treatment comparisons demonstrated superior PFS and response rates with cilta-cel compared with 2 belamaf-containing regimens (BVd and BPd) in patients with RRMM

Conclusions

In the absence of head-to-head trials, indirect treatment comparisons of CARTITUDE-4 vs DREAMM-7 and DREAMM-8 demonstrated statistically significant superior PFS with cilta-cel compared with BVd and BPd

Cilta-cel also demonstrated statistically significant improvements in ≥CR and ≥VGPR response rates compared with BVd and BPd

These analyses adjusting for differences between CARTITUDE-4 vs DREAMM-7 and DREAMM-8 patient populations support IMWG guidance recommending anti-BCMA T-cell receptor therapies prior to ADCs

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Poster

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Disclosures

CS has no disclosures or competing interests to report.

Introduction

- CARTITUDE-4 compared cilta-cel, a chimeric antigen receptor T-cell treatment targeting B-cell maturation antigen (BCMA), with physician's choice between 2 standard of care regimens in lenalidomide-refractory patients with RRMM who received 1–3 prior lines of therapy (LOT), including an immunomodulatory agent and a proteasome inhibitor (PI)[1,2]
  - Cilta-cel demonstrated significantly improved overall survival (OS) and progression-free survival (PFS) (hazard ratio [HR]: OS, 0.55; PFS, 0.29)[2]
- Belamaf, an anti-BCMA antibody-drug conjugate (ADC), in combination with bortezomib and dexamethasone (BVd) and in combination with pomalidomide and dexamethasone (BPd) were evaluated in DREAMM-7 and DREAMM-8, respectively[3,4]
  - Both trials demonstrated improved survival and response rates with belamaf in patients with RRMM who received ≥1 prior LOT[3,4]
- International Myeloma Working Group (IMWG) guidelines recommend anti-BCMA T-cell redirecting therapy, such as cilta-cel, before anti-BCMA ADCs such as belamaf[5]; however, there is no head-to-head comparison on the efficacy of cilta-cel vs belamaf
- This analysis reports matching-adjusted indirect comparisons (MAICs) to estimate the relative efficacies of cilta-cel vs BVd and BPd using CARTITUDE-4 individual patient data (IPD) and published data from DREAMM-7 and DREAMM-8

Methods

- Unanchored MAICs were performed between apheresed patients from the CARTITUDE-4 trial cilta-cel arm (data cut-off: May 2024) and patient populations from the DREAMM-7 and DREAMM-8 trials (data cut-off: October 2023 and January 2024, respectively)
- Eligibility criteria from DREAMM-7 and DREAMM-8 were applied to the cilta-cel IPD, and outcomes for the matched population were compared against published summary data for DREAMM-7 and DREAMM-8
- Imbalances in patient characteristics were adjusted for by weighting IPD from CARTITUDE-4, matching on reported clinically relevant baseline characteristics from DREAMM-7 and DREAMM-8, including cytogenetic risk, International Staging System (ISS) stage, presence of extramedullary disease, and prior LOT (for both trials) and refractory status (for DREAMM-8 only)
- Clinical outcomes analyzed were PFS, complete response (CR) or better, very good partial response (VGPR) or better, and overall response rates (ORRs); these were compared using weighted IPD for cilta-cel and simulated IPD using published Kaplan-Meier PFS curves and reported response rates for BVd and BPd
  - Sensitivity analyses additionally adjusting for age, prior autologous HCT, race, sex, Ig subtype (for both trials), and ECOG PS score (for DREAMM-8 only) were also performed
- For PFS, HRs and 95% CIs were estimated with a weighted Cox proportional hazards model, and relative response ratios (RRs) and 95% CIs were derived from a weighted logistic regression analysis to compare response rates

Results

Patient characteristics

- In total, 208 apheresed patients were included from the CARTITUDE-4 cilta-cel arm, while 243 patients were included from DREAMM-7 and 155 patients from DREAMM-8 (**Table 1**)
- Patients from the CARTITUDE-4 cilta-cel arm who would not have been eligible for DREAMM-7 (n=87) and DREAMM-8 (n=55) were excluded, as CARTITUDE-4 included patients refractory to anti-CD38 (n=50) who would not have been eligible DREAMM-7, and patients refractory to bortezomib who would not have been eligible for both DREAMM-7 (n=55) and DREAMM-8 (n=55)
  - After exclusion, 121 cilta-cel patients remained in the MAIC with BVd and 153 remained in the MAIC with BPd

Table 1: Baseline characteristics, observed and after base case matching to comparator trials

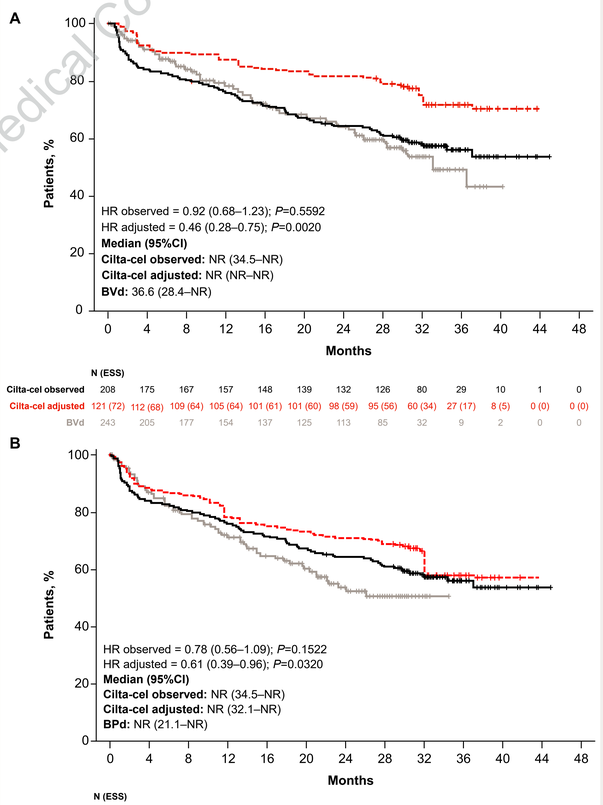
Patient characteristics		CART-4 (N=208)	DREAMM-7 (N=243)	CART-4 adjusted to DREAMM-7 (n=121; ESS=72)	DREAMM-8 (N=155)	CART-4 adjusted to DREAMM-8 (n=153; ESS=76)
High cytogenetic risk,[a,b] %		59	28	28	34	34
R-ISS stage,[a] %	1	21	42	42	NP	-
	2	75	54	54	NP	-
	3	4	4	4	NP	-
Extramedullary disease,[a,b] %		21	5	5	13	13
1 prior LOT,[a,b] %		33	51	51	53	53
Refractory to PI,[b] %		50	NP	-	26	26
Refractory to CD38,[b] %		24	NP	-	23	23
ISS stage,[b] %	1	65	NP	-	61	61
	2	29	NP	-	25	25
	3	6	NP	-	14	14
Age, years, %	≤65	61	50	67	41	67
	≥65 to <75	37	35	29	NP	-
	≥75	3	15	4	NP	-
Prior autologous HCT, %		82	67	87	64	87
ECOG PS status, %	0	55	NP	-	53	64
	1 or 2	45	NP	-	47	36
Race (White), %		87	85	89	86	90
Male, %		56	53	63	64	59
Ig subtype, %	IgA	18	-	-	27	15
	IgG	54	66	55	55	57
Median time from diagnosis to randomization,[c] years		3.0	4.3	2.9	4.0	3.0

[a]Matched in DREAMM-7 base case. [b]Matched in DREAMM-8 base case. [c]Time from diagnosis to randomization was not included in the base case or sensitivity analyses.
CART-4, CARTITUDE-4; ECOG PS, Eastern Cooperative Oncology Group performance status; HCT, hematopoietic cell transplantation; Ig, immunoglobulin; NP, not published; R-ISS, Revised International Staging System.

Progression-free survival

- Following adjustment, cilta-cel was associated with prolonged PFS compared with BVd and BPd (**Figure 1**)
  - Cilta-cel demonstrated improvements in PFS, with a 54% and 39% lower risk of disease progression or death than BVd and BPd, respectively
- Sensitivity analyses showed generally consistent results with the base case adjusted comparison

Figure 1: PFS for cilta-cel vs (A) BVd and (B) BPd



NR, not reached.

Treatment response

- Cilta-cel showed statistically significant superior depth of response with a 51.4%-point difference in ≥CR and a 23.9%-point difference in ≥VGPR compared with BVd (**Table 2** and **Figure 2**) and a 41.8%-point difference in ≥CR and a 22.7%-point difference in ≥VGPR compared with BPd (**Table 3** and **Figure 2**); all *P*<0.0001
- Cilta-cel demonstrated a significantly higher ORR with a 10.2%-point difference compared with BVd and a 11.9%-point difference compared with BPd

Table 2: Treatment response of BVd and cilta-cel adjusted to BVd

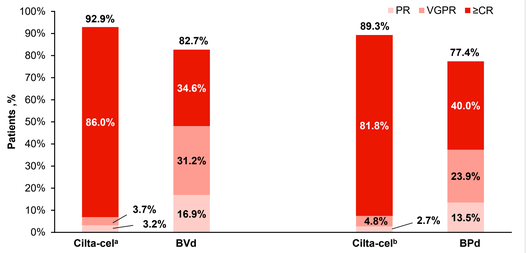
Outcome	Cilta-cel adjusted to BVd, %	BVd, %	% difference cilta-cel adjusted vs BVd	RR (95% CI)	*P* value
≥CR	86.0	34.6	**+51.4**	2.49 (2.04–3.03)	<0.0001
≥VGPR	89.7	65.8	**+23.9**	1.36 (1.21–1.53)	<0.0001
ORR	92.9	82.7	**+10.2**	1.12 (1.03–1.22)	0.009

In the cilta-cel observed cohort, ≥CR was 76.9%, ≥VGPR was 81.3%, and ORR was 84.6%; differences in percentage with cilta-cel adjusted vs BVd that are significant are shown in bold.

Table 3: Treatment response of BPd and cilta-cel adjusted to BPd

Outcome	Cilta-cel adjusted to BPd, %	BPd, %	% difference cilta-cel adjusted vs BPd	RR (95% CI)	*P* value
≥CR	81.8	40.0	**+41.8**	2.05 (1.65–2.53)	<0.0001
≥VGPR	86.6	63.9	**+22.7**	1.36 (1.18–1.56)	<0.0001
ORR	89.3	77.4	**+11.9**	1.15 (1.04–1.29)	0.010

Figure 2: Treatment response of BVd and BPd and cilta-cel adjusted to BVd and adjusted to BPd



[a]Adjusted to DREAMM-7. [b]Adjusted to DREAMM-8. PR, partial response.

- Sensitivity analyses showed consistent results with the base case adjusted comparison

Limitations

- There were substantial differences in patient populations in CARTITUDE-4 vs DREAMM-7 and DREAMM-8; however, sizes of the adjusted cilta-cel cohort remained large enough for robust comparisons in the base case that showed statistically significant differences across efficacy outcomes
- As with any nonrandomized comparisons, potential unmeasured residual confounding cannot be excluded. However, sensitivity analyses adjusting for a wider set of baseline characteristics show comparative estimates, though CIs widened due to decreased ESS

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Multiple Myeloma

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