Efficacy of CARVYKTI in CARTITUDE-4 versus Other Conventional Treatment Regimens for Lenalidomide-Refractory Multiple Myeloma Patients Using Inverse Probability of Treatment Weighting

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Presented by R Fonseca at the 66th American Society of Hematology (ASH) Annual Meeting; December 7–10, 2024; San Diego, CA, USA

Introduction

- Cilta-cel demonstrated superior PFS, OS, and response rates over DPd or PVd in patients with RRMM who are refractory to lenalidomide and have received 1-3 prior LOTs including an IMiD and a PI, in the phase 3 randomized CARTITUDE-4 trial[1]
- Comparative efficacy was previously assessed for cilta-cel versus other frequently used treatment regimens in this setting–DVd, DKd, Kd, and Pd–using available patient-level data[2]
- Data from a later prespecified data-cut of CARTITUDE-4 with median follow-up of 34 months became available,[1] allowing for an updated assessment of the comparative efficacy, including OS, between cilta-cel and these treatment regimens
- We assessed the comparative efficacy of cilta-cel versus DVd, DKd, Kd, and Pd for patients with lenalidomide-refractory multiple myeloma

cilta-cel, ciltacabtagene autoleucel; DKd, daratumumab, carfilzomib, and dexamethasone; DPd, daratumumab, pomalidomide, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; IMiD, immuno-modulatory agent; Kd, carfilzomib and dexamethasone; LOT, line(s) of therapy; OS, overall survival; Pd, pomalidomide and dexamethasone; PFS, progression-free survival; PI, proteasome inhibitor; PVd, pomalidomide, bortezomib, and dexamethasone; RRMM, relapsed and refractory multiple myeloma.

1. Mateos MV, et al. Presented at the 21st IMS Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil. Abstract OA-65. Alsdorf W, et al. *Journal of Comparative Effectiveness Research*, 13(9), e240080.

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Methods

Data Sources and Population

- IPD were collected from the following randomized trials, and analysis was restricted to patients who met CARTITUDE-4 eligibility criteria at enrollment and had no prior exposure to anti-CD38 therapies:
  - CARTITUDE-4 (cilta-cel; median follow-up 34 months)
  - CASTOR (DVd; median follow-up 73 months)
  - CANDOR (DKd and Kd; median follow-up 50 months)
  - APOLLO (Pd; median follow-up 40 months)

Adjustment and Outcomes

- Imbalances on key patient characteristics between cohorts were adjusted for using IPTW
- Patients in the comparator cohorts were reweighted using ATT weighting
- Outcomes: PFS, OS, and response rates (ORR, ≥VGPR, and ≥CR)

ATT, average treatment effect in the treated; cilta-cel, ciltacabtagene autoleucel; CR, complete response; DKd, daratumumab, carfilzomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; IPD, individual patient data; IPTW, inverse probability of treatment weighting; Kd, carfilzomib and dexamethasone; ORR, overall response rate; OS, overall survival; Pd, pomalidomide and dexamethasone; PFS, progression-free survival.

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Population Adjustment

- The analysis included 155 patients in the cilta-cel arm; comparator cohorts consisted of patients treated with DVd (n=44), DKd (n=98), Kd (n=46), and Pd (n=92) who met the CARTITUDE-4 inclusion criteria
- The majority of baseline covariates were well balanced across the cohorts after IPTW
- Imbalances remained between cohorts for proportion of patients with EMD (SMD ≥0.25) after IPTW due to few patients in the comparator cohorts with EMD, suggesting that results are conservative for cilta-cel

Key Prognostic Baseline Characteristics Before and After Adjustment with IPTW

Variable	Categories	Cilta-cel	DVd			DKd			Kd			Pd		
		N = 155 N (%)	Unadjusted N = 44 N (%)	IPTW N = 36 N (%)	SMD*	Unadjusted N = 98 N (%)	IPTW N = 85 N (%)	SMD*	Unadjusted N = 46 N (%)	IPTW N = 42 N (%)	SMD*	Unadjusted N = 92 N (%)	IPTW N = 71 N (%)	SMD*
Refractory status	< Double refractory ≥ Double refractory	82 (52.9) 73 (47.1)	18 (40.9) 26 (59.1)	18 (49.5) 18 (50.5)	-0.068	54 (55.1) 44 (44.9)	46 (53.4) 40 (46.6)	0.009	26 (56.5) 20 (43.5)	23 (53.9) 19 (46.1)	0.021	45 (48.9) 47 (51.1)	37 (52.1) 34 (47.9)	-0.015
ISS stage	I II III	103 (66.5) 44 (28.4) 8 (5.2)	19 (43.2) 15 (34.1) 10 (22.7)	24 (66.7) 10 (28.7) 2 (4.6)	0.026	51 (52.0) 28 (28.6) 19 (19.4)	57 (67.2) 23 (27.2) 5 (5.6)	0.030	23 (50.0) 15 (32.6) 8 (17.4)	28 (65.5) 12 (29.3) 2 (5.1)	0.021	41 (44.6) 33 (35.9) 18 (19.6)	48 (68.1) 19 (26.8) 4 (5.1)	0.037
Time to progression on prior line	< 6 months ≥ 6 months	22 (14.2) 133 (85.8)	7 (15.9) 37 (84.1)	4 (11.0) 32 (89.0)	-0.095	20 (20.4) 78 (79.6)	12 (14.6) 73 (85.4)	0.010	14 (30.4) 32 (69.6)	5 (12.2) 37 (87.8)	-0.059	19 (20.7) 73 (79.3)	10 (14.3) 61 (85.7)	0.002
EMD	Yes No	29 (18.7) 126 (81.3)	1 (2.3) 43 (97.7)	2 (4.5) 34 (95.5)	-0.455	5 (5.1) 93 (94.9)	7 (7.7) 79 (92.3)	-0.329	3 (6.5) 43 (93.5)	4 (9.2) 38 (90.8)	-0.277	3 (3.3) 89 (96.7)	4 (5.5) 67 (94.5)	-0.415

*SMD between the cilta-cel cohort and the comparator cohort following adjustment.
cilta-cel, ciltacabtagene autoleucel; DKd, daratumumab, carfilzomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; EMD, plasmacytoma/extramedullary disease; IPTW, inverse probability of treatment weighting; ISS, International staging system; Kd, carfilzomib and dexamethasone; Pd, pomalidomide and dexamethasone; SMD, standardized mean difference.

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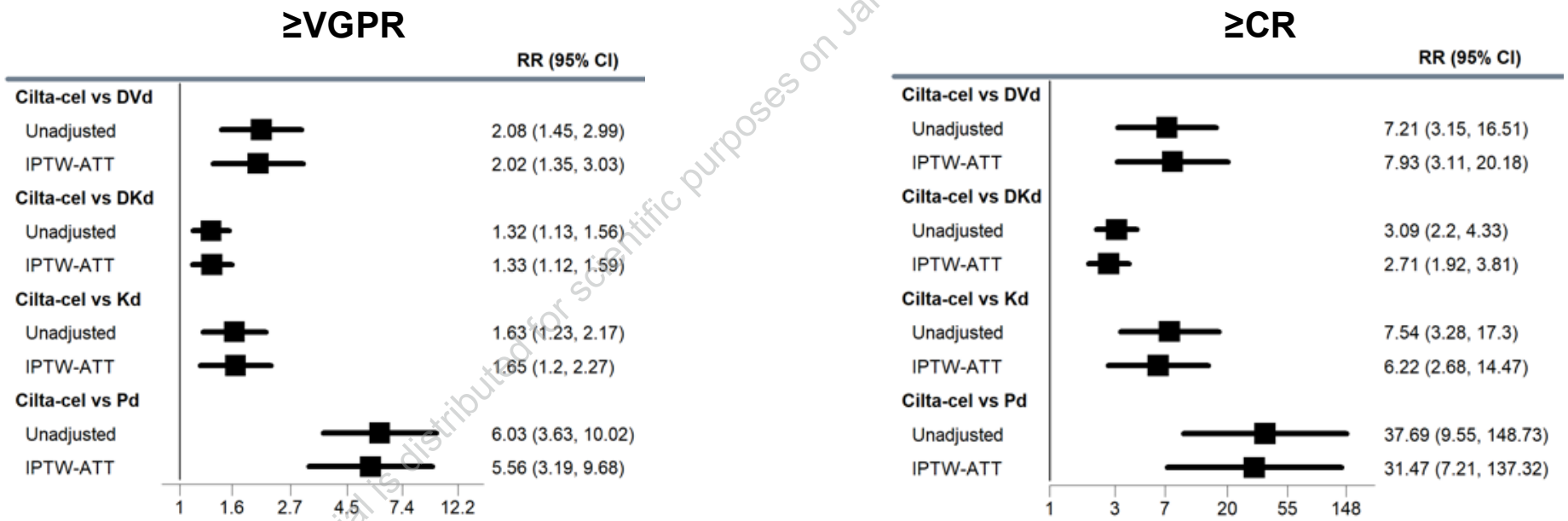
Response

- Following adjustment, cilta-cel demonstrated a significantly increased chance of patients achieving:
  - ≥VGPR: 1.3- fold vs DKd, 1.7-fold vs Kd, 2.0-fold vs DVd, and 5.6-fold vs Pd
  - ≥CR: 2.7-fold vs DKd, 6.2-fold vs Kd, 7.9-fold vs DVd, and 31.5-fold vs Pd
- Consistent results were obtained in all sensitivity analyses



HR<1 and RR>1 indicates favorable treatment effect for cilta-cel.
ATT, average treatment effect in the treated; CI, confidence interval; cilta-cel, ciltacabtagene autoleucel; CR, complete response; DKd, daratumumab, carfilzomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; HR, hazard ratio; IPTW, inverse probability of treatment weighting; Kd, carfilzomib and dexamethasone; Pd, pomalidomide and dexamethasone; RR, rate ratio; VGPR, very good partial response.

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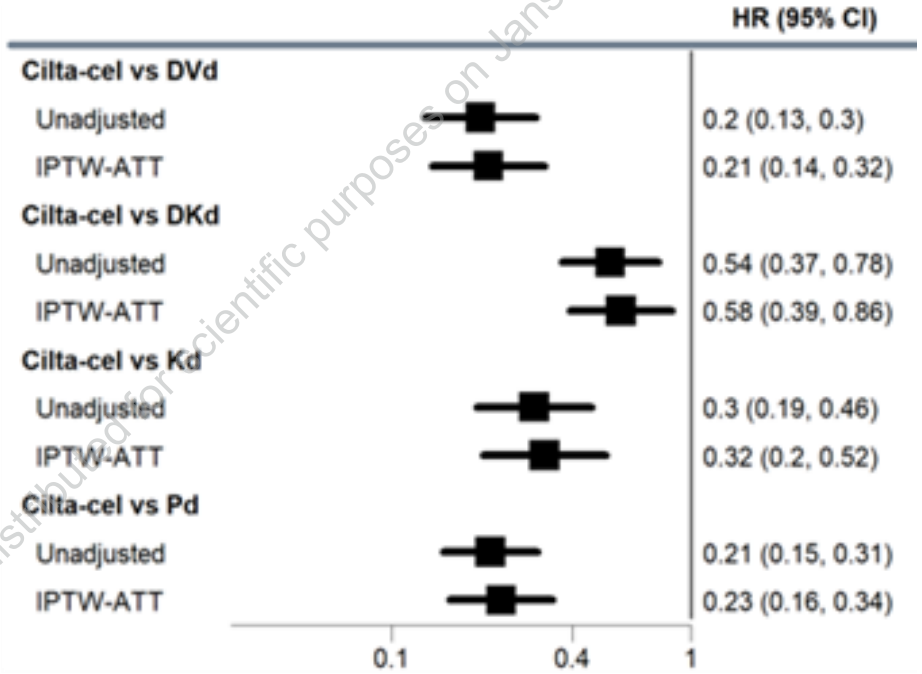
Progression-Free Survival

- Following adjustment, cilta-cel was associated with a significant reduction in the risk of disease progression or death, by 42% vs DKd, 68% vs Kd, 77% vs Pd, and 79% vs DVd
- Consistent results were obtained in all sensitivity analyses

Comparative PFS for Cilta-cel vs DVd, DKd, Kd, Pd



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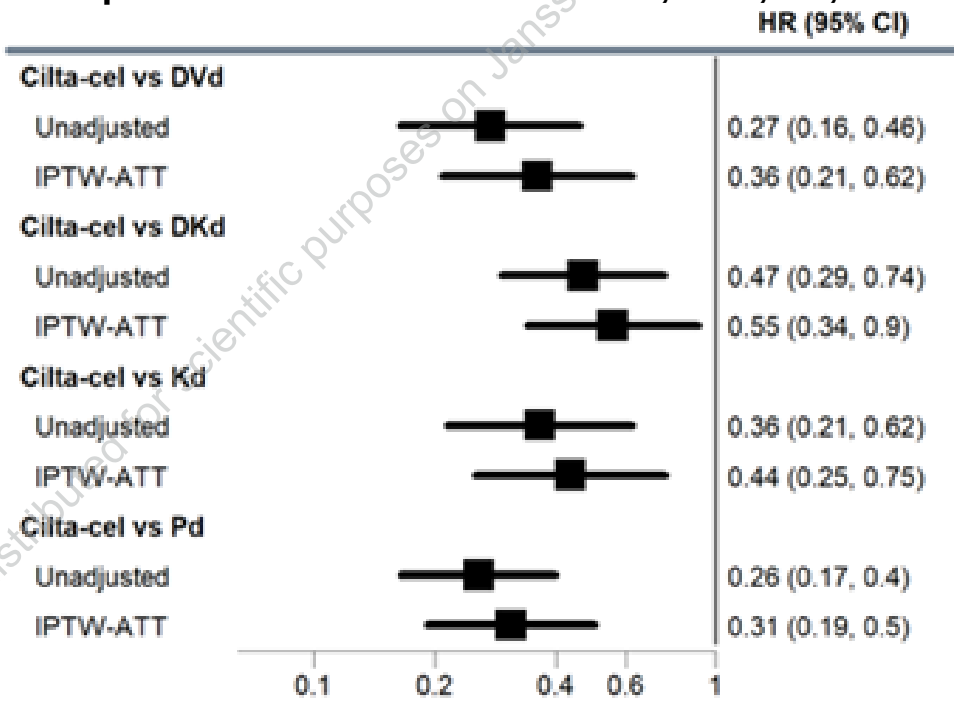
Overall Survival

- Following adjustment, cilta-cel was associated with a significant reduction in the risk of death, by 45% vs DKd, 56% vs Kd, 64% vs DVd, and 69% vs Pd
- Consistent results were obtained in all sensitivity analyses

Comparative OS for Cilta-cel vs DVd, DKd, Kd, Pd



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ATT, average treatment effect in the treated; CI, confidence interval; cilta-cel, ciltacabtagene autoleucel; DKd, daratumumab, carfilzomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; HR, hazard ratio; IPTW, inverse probability of treatment weighting; Kd, carfilzomib and dexamethasone; OS, overall survival; Pd, pomalidomide and dexamethasone.

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Conclusions

- Cilta-cel showed superior efficacy across response and survival outcomes compared to other common treatments for patients with lenalidomide-refractory RRMM who received 1-3 prior LOT, including a PI and IMiD
- This analysis with longer follow-up strengthens the previously published results comparing cilta-cel to these treatments, and the new OS results highlight the added value of cilta-cel in this population
- These findings further confirm that cilta-cel is an effective treatment for patients with lenalidomide-refractory RRMM who received 1-3 prior LOT, including a PI and IMiD

Based on this updated analysis, cilta-cel demonstrates significantly greater benefit across all efficacy outcomes, including overall survival, compared to conventional treatments (DVd, DKd, Kd, and Pd) for patients with lenalidomide-refractory multiple myeloma as early as second line

cilta-cel, ciltacabtagene autoleucel; DKd, daratumumab, carfilzomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; IMiD, immuno-modulatory agent; Kd, carfilzomib and dexamethasone; LOT, line(s) of therapy; ORR, overall response rate; OS, overall survival; Pd, pomalidomide and dexamethasone; PI, proteasome inhibitor; PFS, progression-free survival; RRMM, relapsed and refractory multiple myeloma; VGPR, very good partial response.

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