Updated Comparative Efficacy of Ciltacabtagene Autoleucel Versus Idecabtagene Vicleucel in Patients With Relapsed or Refractory Multiple Myeloma Previously Treated With 2–4 Prior Lines of Therapy Using a Matching-Adjusted Indirect Comparison

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Introduction

- CARVYKTI (cilta-cel) and Abecma (ide-cel) are BCMA-targeting CAR-T cell therapies approved for the treatment of patients with RRMM who have received at least 1 (cilta-cel) or 2 (ide-cel) prior LOTs[1,2]
  - In CARTITUDE-4, cilta-cel showed superior OS compared to SOC in patients with RRMM who are refractory to lenalidomide and received 1–3 prior LOTs, including an IMiD and a PI (HR, 0.55; 95% CI, 0.39–0.79)[3]
  - In KarMMa-3, a statistically significant improvement in OS has yet to be demonstrated for ide-cel vs SOC in the ITT population for TCE RRMM with 2–4 prior LOTs (HR, 1.01; 95% CI, 0.73–1.40)[4]
- A previous MAIC of cilta-cel vs ide-cel showed significant clinical benefit for cilta-cel over ide-cel across response outcomes and PFS for patients with TCE RRMM treated with 2–4 prior LOTs[5]; results for OS were not available
- The objective of this analysis was to assess cilta-cel vs ide-cel using longer follow-up data from CARTITUDE-4 and KarMMa-3, including OS[3,4]

BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; ide-cel, idecabtagene vicleucel; IMiD, immunomodulatory drug; LOT, line of therapy; MAIC, matching-adjusted indirect comparison; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma; SOC, standard of care; TCE, triple-class exposed.

1. Johnson & Johnson. April 5, 2024. CARVYKTI is the first and only BCMA-targeted treatment approved by the US FDA for patients with relapsed or refractory multiple myeloma who have received at least one prior line of therapy. News release. 2. Bristol Myers Squibb and 2seventy bio, Inc. April 4, 2024. US FDA approves Bristol Myers Squibb and 2seventy bio's Abecma for triple-class exposed relapsed or refractory multiple myeloma after two prior lines of therapy. 3. Mateos MV et al. Presented at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil. 4. Ailawadhi, et al. *Blood.* 2024. doi: https://doi.org/10.1182/blood.2024024582. 5. Bar, N., et al. *Blood.* 2023;142:2141.

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Methods

- Given the availability of IPD for cilta-cel and only published aggregate data for ide-cel from KarMMa-3, and due to the absence of a common comparator, an unanchored MAIC was performed
- Patients in CARTITUDE-4 and CARTITUDE-1 who fulfilled the inclusion criteria from KarMMA-3 were selected
- Additional imbalances in patient characteristics were adjusted for by weighting the cilta-cel IPD to match the reported baseline characteristics of KarMMa-3
  - Prognostic factors to be adjusted for were identified *a priori*
  - The factors in the base-case analysis were selected based on ability to match factors ranked most important while maintaining a sufficient ESS
  - A sensitivity analysis that adjusted for additional prognostic factors was also conducted

Analysis sets for KarMMa-3 and CARTITUDE-4/CARTITUDE-1

<table>
<tr><th>Ide-cel</th><th colspan="2">Cilta-cel</th></tr>
<tr><td rowspan="3">KarMMa-3
(N=254)</td><td>CARTITUDE-4 (N=208)</td><td>CARTITUDE-1 patients with 3–4 prior LOTs (N=37)</td></tr>
<tr><td colspan="2">CARTITUDE-1 + CARTITUDE-4 (N=245)</td></tr>
<tr><td colspan="2">KarMMa-3 eligibility criteria applied: Patients with only 1 prior LOT or no prior daratumumab were excluded, leaving N=85 included in the cilta-cel cohort (CARTITUDE-1, 36; CARTITUDE-4, 49)</td></tr>
</table>

cilta-cel, ciltacabtagene autoleucel; ESS, effective sample size; ide-cel, idecabtagene vicleucel; IPD, individual patient-level data; LOT, line of therapy; MAIC, matching-adjusted indirect comparison.

Baseline Characteristics Before and After Population Adjustment

- 85 patients were included in the cilta-cel cohort after applying the KarMMa-3 inclusion and exclusion criteria
- After population adjustment, the baseline characteristics of the cilta-cel cohort matched the reported average baseline characteristics of the ide-cel population from KarMMa-3

Baseline characteristics[a] matched: base case

Baseline characteristics matched		Cilta-cel observed N=245	Ide-cel observed N=254	Cilta-cel adjusted (N=79[b]; ESS=39[c])
Refractory status	Refractory to lenalidomide	97%	73%	73%
	Non-triple refractory	76%	35%	35%
	Triple-/quadruple-refractory	19%	59%	59%
	Penta-refractory	5%	6%	6%
	Refractory to PI	55%	74%	74%
	Refractory to CD38	36%	95%	95%
Cytogenetic risk	High risk	54%	42%	42%
R-ISS stage	I	24%	22%	22%
	II	71%	65%	65%
	III	5%	13%	13%
Time to progression	Median TTP on last treatment (months)	13.8	7.1	7.3
EMD	Yes	20%	24%	24%
Tumor burden	High	27%	28%	28%

Additional baseline characteristics[a] adjusted: sensitivity analysis

Baseline characteristics matched		Cilta-cel observed N=245	Ide-cel observed N=254	Cilta-cel adjusted (N=79[b]; ESS=32[d])
Prior lines	Median number	2	3	3
Time from diagnosis to screening	Median time from diagnosis to screening (years)	3.2	4.1	4.4
Age	<65	61%	59%	50%
	65 to 75	36%	36%	48%
	≥75	3%	5%	2%
Prior transplant	Yes	83%	84%	88%
ECOG PS	1+	48%	53%	53%
Race	White	84%	86%	85%
	Black	6%	9%	9%
	Other	10%	5%	6%
Sex	Male	57%	61%	56%

[a]For pooled CARTITUDE-4/CARTITUDE-1 and KarMMa-3 analysis sets. [b]An additional 6 patients in the cilta-cel cohort were excluded due to missing values in baseline characteristics for adjustment. [c]In the base case analysis, ESS=39 after weighting; ESS is reflective of the weighted population. [d]In the sensitivity analysis, ESS=32 after additional baseline characteristics were adjusted for; ESS is reflective of the weighted population.
cilta-cel, ciltacabtagene autoleucel; EMD, extramedullary disease; ECOG PS, Eastern Cooperative Oncology Group Performance Status Score; ESS, effective sample size; ide-cel, idecabtagene vicleucel; PI, proteasome inhibitor; R-ISS, Revised International Staging System; TTP, time to progression.

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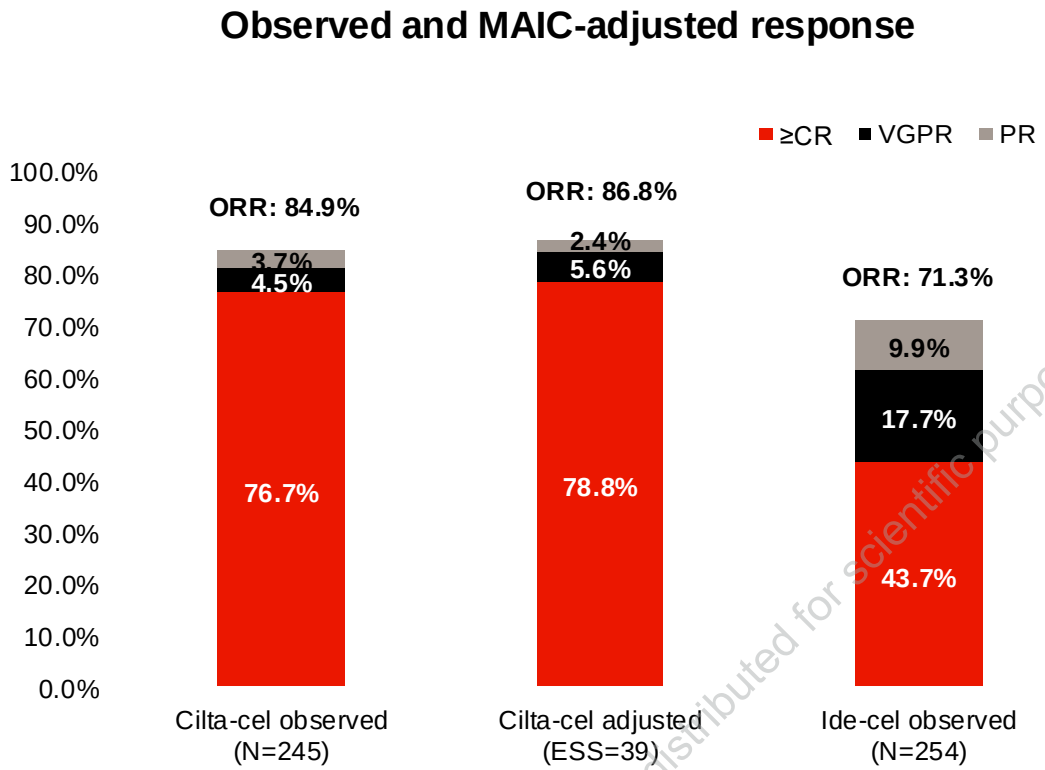
Patients Who Received Cilta-cel Were More Likely to Respond to Treatment and to Achieve Deep Responses



	Response			Comparative Efficacy of Response Cilta-cel vs Ide-cel RR[a] (95% CI)	
	Cilta-cel		Ide-cel		
	Observed	Adjusted	Observed	Adjusted	P-value
ORR	84.9%	86.8%	71.3%	1.22 (1.08, 1.38)	0.0126
≥VGPR	81.2%	84.4%	61.4%	1.37 (1.19, 1.59)	0.0009
≥CR	76.7%	78.8%	43.7%	1.80 (1.49, 2.18)	<0.0001

[a]RR>1 indicates favorable treatment effect for cilta-cel.
cilta-cel, ciltacabtagene autoleucel; CR, complete response; ESS, effective sample size; ide-cel, idecabtagene vicleucel; MAIC, matching-adjusted indirect comparison; ORR, objective response rate; PR, partial response; RR, response rate ratio; VGPR, very good partial response.

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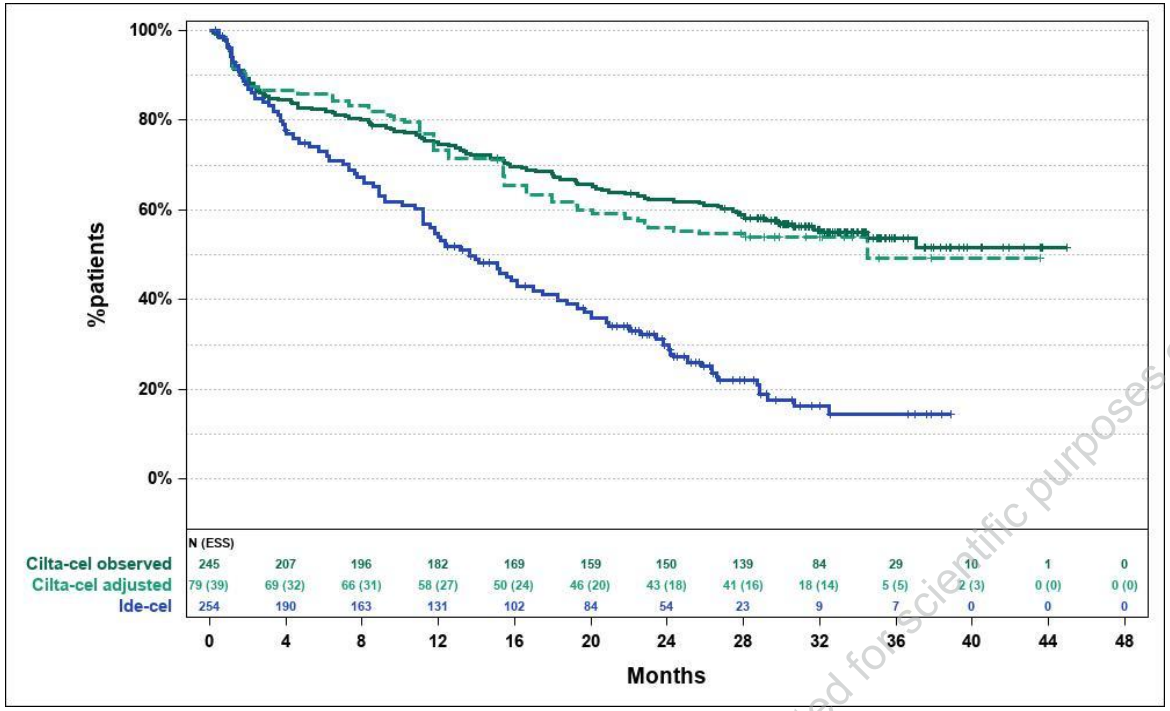
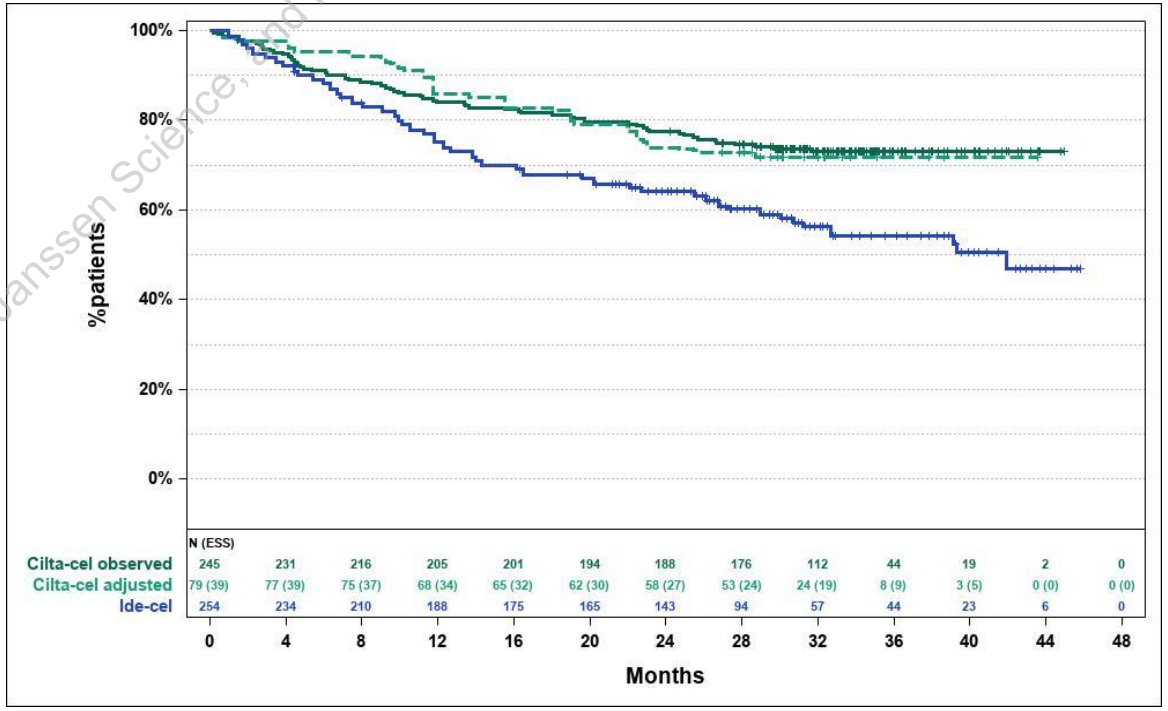
Cilta-cel Was Associated With Reductions in Risk of Disease Progression or Death and in Risk of Death vs Ide-cel

Comparative efficacy of PFS for cilta-cel vs ide-cel



Median, months (95% CI)			Cilta-cel vs Ide-cel HR[a] (95% CI)		
Cilta-cel		Ide-cel			
Observed	Adjusted	Observed	Observed	Adjusted	P-value
NE	34.5 (15.5, NE)	13.7 (11.6, 16.1)	0.39 (0.30, 0.49)	0.42 (0.26, 0.68)	0.0004

Comparative efficacy of OS for cilta-cel vs ide-cel



Median, months (95% CI)			Cilta-cel vs Ide-cel HR[a] (95% CI)		
Cilta-cel		Ide-cel			
Observed	Adjusted	Observed	Observed	Adjusted	P-value
NE	NE	41.9 (31.2, NE)	0.54 (0.40, 0.74)	0.58 (0.34, 0.99)	0.0452

[a]HR<1 indicates favorable treatment effect for cilta-cel.
cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; ide-cel, idecabtagene vicleucel; NE, not estimable; OS, overall survival; PFS, progression-free survival.

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Conclusions

- Cilta-cel showed significant improvements in OS, response outcomes, and PFS compared to ide-cel in patients with TCE RRMM treated with 2–4 prior LOTs
- Comparative results were confirmed for cilta-cel vs ide-cel with longer follow-up, and the new OS results highlight the added value of cilta-cel in this population
- This analysis further demonstrated the superior clinical benefits of cilta-cel compared to ide-cel for patients with TCE RRMM treated with 2–4 prior LOTs

Based on this updated analysis, cilta-cel demonstrates a significant OS benefit compared to ide-cel for patients with TCE RRMM treated with 2–4 prior LOTs

cilta-cel, ciltacabtagene autoleucel; ide-cel, idecabtagene vicleucel; LOT, line of therapy; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma; TCE, triple-class exposed.

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