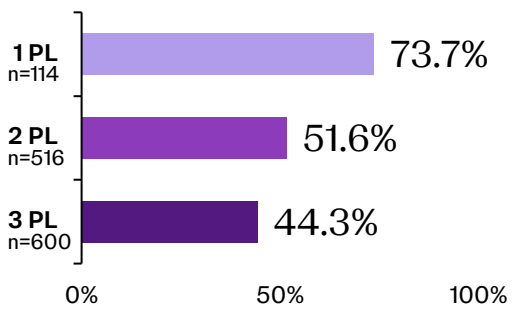
Evidence and value summary: CARVYKTI®

Lenalidomide-refractory relapse/refractory multiple myeloma current with 1-3 prior LOT; challenges and gaps in care

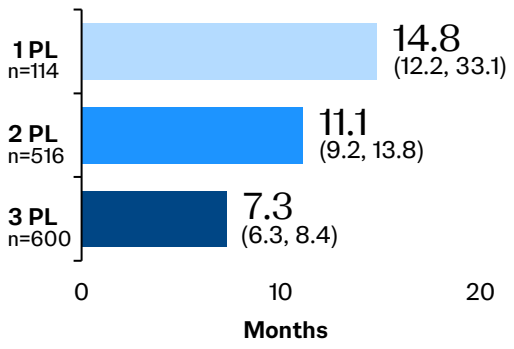
Data below are based on an analysis of patient-level data to characterize treatments and outcomes by number of prior lines (PL) of therapy[a]

Overall response rates by number of PL[1,a]



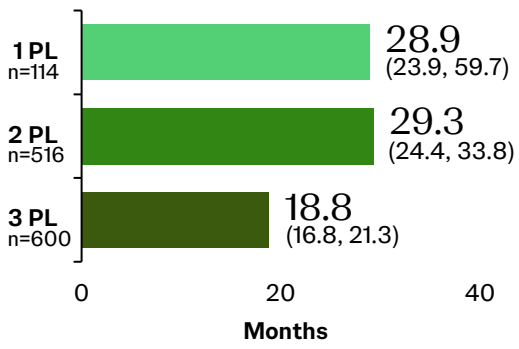
Median PFS rates for each LOT[1,a]

Median (95% CI) PFS, months
Overall: 9.3 (8.3,10.4)



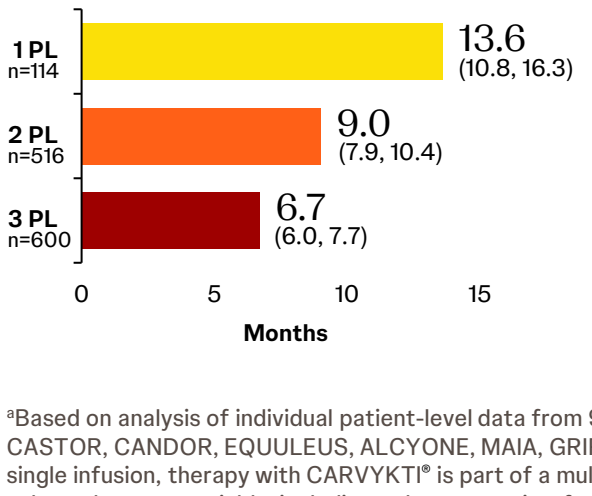
Median OS rates for each LOT[1,a]

Median (95% CI) OS, months
Overall: 23.9 (21.8, 25.8)



Median time to next treatment (TTNT) with each additional LOT[1,a]

Median (95% CI) TTNT, months
Overall: 8.3 (7.7, 9.3)



CARVYKTI®: CAR-T therapy delivered as a one-time infusion in lenalidomide-refractory MM patients who previously received at least 1 prior LOT, including a proteasome inhibitor + immunomodulatory agent[2,3,c]

Approved FDA Indication[4]

CARVYKTI® (ciltacabtagene autoleucel) is a **BCMA-directed** genetically modified autologous **T cell immunotherapy** indicated for treatment of adult patients with **RRMM** who have received at least 1 prior LOT, including a proteasome inhibitor, an immunomodulatory agent, and are refractory to lenalidomide.

Boxed warning:

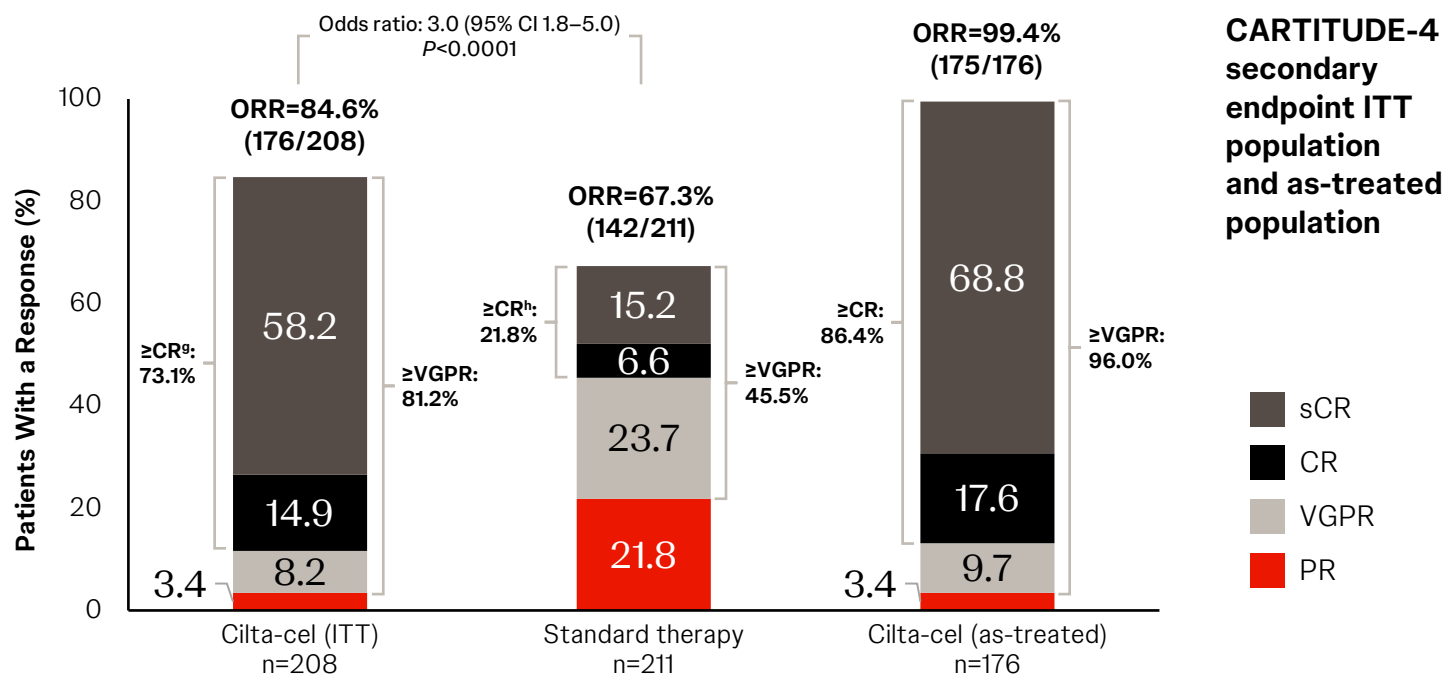
CRS, neurologic toxicities, HLH/MAS, prolonged and recurrent cytopenia, and secondary hematological malignancies[4]

CARVYKTI®: Clinical evidence[2,3]

CARTITUDE-4: A phase 3, randomized, open-label study of cilta-cel vs ST (PVd or DPd) in lenalidomide-refractory MM patients who previously received 1–3 prior LOT, including a PI + IMiD.
(Cilta-cel (ITT) n=208, standard therapy n= 211, and Cilta-cel (as treated) n= 176)

At a median follow-up of 15.9 months, **a single infusion of cilta-cel significantly prolonged PFS vs ST (HR=0.26; *P<0.001*)[d,e]** in lenalidomide-refractory MM patients with 1–3 prior LOT

Overall response rates[f]



CARTITUDE-4	Cilta-cel (ITT) (n = 208)	Standard therapy (n = 211)
Median PFS, months (95% CI)	NR (22.8–NE)	11.8 (9.7–13.8)
	HR: 0.26 (weighted) (95% CI, 0.18–0.38); *P*<0.001[i] HR: 0.40 (unweighted) (95% CI, 0.29-0.55); P<0.001[i]	
MRD negativity[j], %	60.6	15.6
	OR: 8.7[k] (95% CI, 5.4–13.9); *P*<0.0001[l]	

Selected safety profile[3]

Please refer to the full prescribing information for a complete listing of all adverse events, including other serious adverse events.

Any grade CRS:

134/176 pts (76.1%)

- Grade 1 or 2: 132 pts (75%)
- Grade 3: 2 pts (1.1%)
- Grade 4: 0 pts
- Median time to onset: 8.0 days (1–23)
- Median duration: 3 days (1–17)

Any grade ICANS:

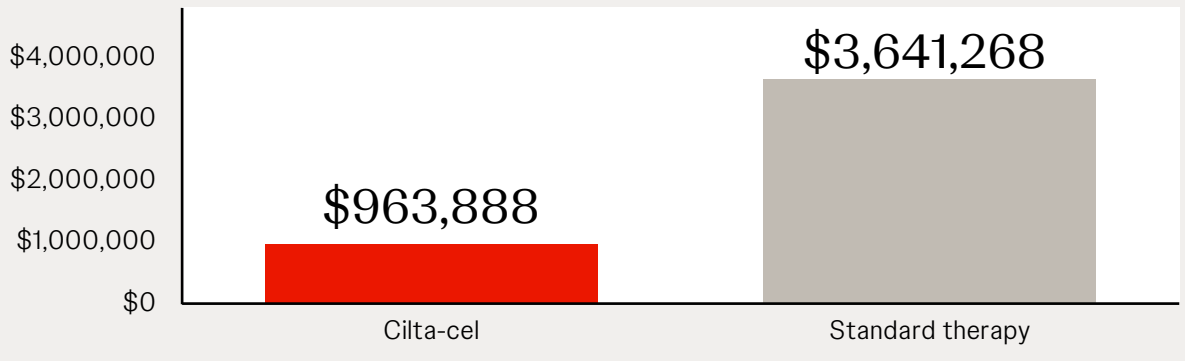
8/176 pts (4.5%)

- Grade 1 or 2: 8 pts (4.5%)
- Grade 3: 0 pts
- Grade 4: 0 pts
- Median time to onset: 9.5 days (6–15)
- Median duration: 2.0 days (1-6)

CARVYKTI®: Economic considerations[5]

CPR analysis of data from CARTITUDE-4, **costs were lower compared to standard therapy (DPd or PVd).**

Base-case cost per complete responder results over 25.4 months



[a]Based on analysis of individual patient-level data from 9 clinical trials from the daratumumab clinical development program including all treatment arms (with and without daratumumab; included APOLLO, CASTOR, CANDOR, EQUULEUS, ALCYONE, MAIA, GRIFFIN, POLLUX, and CASSIOPEIA). [b]Based on analysis of the SEER-Medicare database from 1/2007-12/2019 & 1/2016 onward. [c]Although delivered as a single infusion, therapy with CARVYKTI® is part of a multi-step process. [d]Constant piecewise weighted log-rank test. [e]Hazard ratio and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable, including only progression-free survival events that occurred >8 weeks post-randomization. [f]Assessed using a validated computerized algorithm; ORR is defined as the proportion of subjects who achieve a PR or better per IMWG criteria. [g]*P*-value from the Cochran Mantel-Haenszel Chi-Squared test. [h]Odds ratio: 10.3; *P*<0.0001. [i]Stratified log-rank test. [j]Accessed at a threshold of $1x10^{-5}$ by next generation sequencing available for 126 of 144 patients (87.5%) cilta-cel and 33 of 101 patients (32.7%) standard of care group. [k]Stratified Cochran Mantel-Haenszel test. [l]Fisher's Exact Test. AE, adverse event, BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T-cell; CI, confidence interval; CPR, cost per responder; CR, complete response; CRS, cytokine release syndrome; DoR, duration of response; DPd, daratumumab, pomalidomide, and dexamethasone; HR, hazard ratio; ICANS, immune effector cell–associated neurotoxicity syndrome; LOT, line of therapy; MRD, minimal residual disease; MNT, movement and neurocognitive treatment-emergent adverse events; NE, not evaluable; NR, not reached; OL, open label; OR, odds ratio; ORR, overall response rate; OS, overall survival; PFS, progression free survival; PI, protease inhibitor; PL, prior line; PVd, pomalidomide, bortezomib, and dexamethasone; ST, standard therapy; TEAE, treatment emergent adverse event.

1. Dhakal B, et al. Presented at ASH 2022 annual meeting; Dec 10–13, 2022. Poster Presentation 1883. 2. Dhakal B, et al. Presented at ASCO Annual Meeting; June 2–6, 2023. Oral presentation LBA106. 3. San-Miguel J, et al. *N Engl J Med*. 2023;389(4):335-347. 4. CARVYKTI® (ciltacabtagene autoleucel) [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 5. Data on file. Janssen Biotech, Inc. 6. Rodriguez-Otero P, et al. *N Engl J Med*. 2023;88:1002–1014. 7. Abecma® (idecabtagene vicleucel) [Prescribing Information]. Summit, NJ. Bristol-Myers Squibb and Cambridge, MA. bluebird bio, Inc

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