ASCO 2023 Investor Meeting

June 5, 2023

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Agenda

Introduction	**Dr. Ying Huang, CEO**
CARTITUDE-4	Dr. Binod Dhakal, Medical College of Wisconsin
CARTITUDE-1 & LEGEND-2	Dr. Shambavi Richard, Mount Sinai
Q&A	
Breakfast	

Introduction

Binod Dhakal, M.D.
Associate Professor
Cancer Center - Froedtert Hospital
Medical College of Wisconsin

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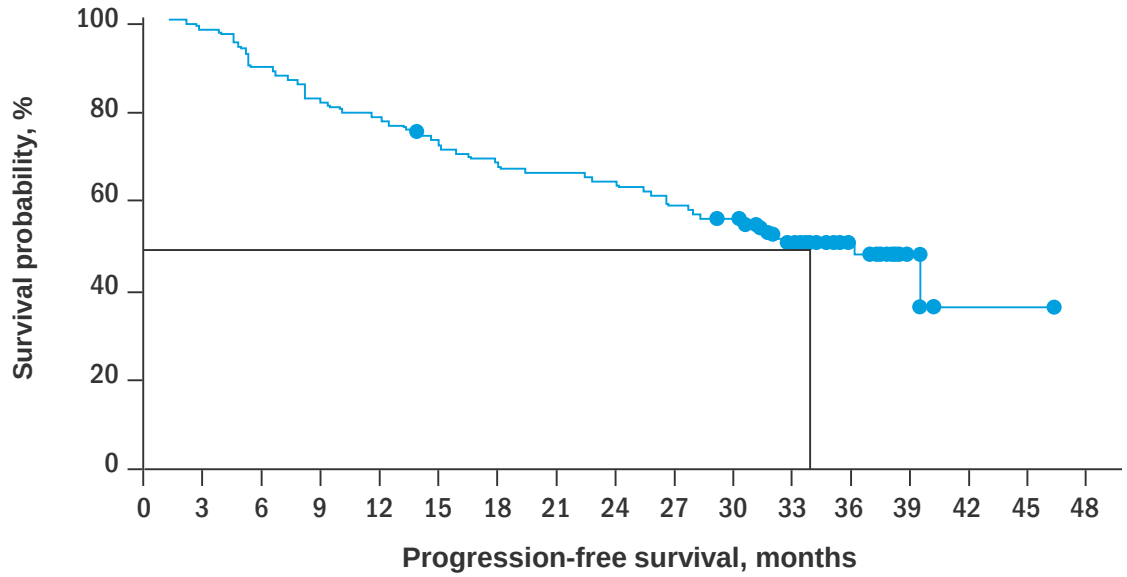
Associate Professor of Medicine (Hematology & Medical Oncology)
Center of Excellence for Multiple Myeloma, Mount Sinai

CARTITUDE-4

Phase 3 Results: Cilta-cel Versus Standard of Care (PVd or DPd) in Lenalidomide-Refractory Multiple Myeloma

CARTITUDE-4: Introduction

- Cilta-cel is a **dual-binding**, BCMA-directed CAR-T therapy
- The phase 1b/2 **CARTITUDE-1** study has shown a median PFS of ~3 years **in heavily pretreated** patients with MM with ≥3 prior LOT
- We aimed to test cilta-cel in **earlier lines** against effective SOC treatments
  - In real-world studies, patients with lenalidomide-refractory disease often have median PFS <12 months[1]
- **The phase 3 CARTITUDE-4 study compared cilta-cel vs physician's choice of either DPd or PVd in patients with lenalidomide-refractory MM after 1–3 prior LOT[2]**
  - This represents a patient population with clear unmet need commonly seen in clinical practice
  - Median follow-up was 15.9 months



See Poster #8009 at ASCO for details
Presented June 5, 2023 8:00–11:00 AM
Discussion 3:00–4:30 PM

BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; cilta-cel, ciltacabtagene autoleucel; DPd, daratumumab, pomalidomide, and dexamethasone; len, lenalidomide; LOT, line of therapy; MM, multiple myeloma; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone; SOC, standard of care.

1. de Arriba de la Fuente F, et al. *Cancers* 2023;15:155. 2. ClinicalTrials.gov. NCT04181827.

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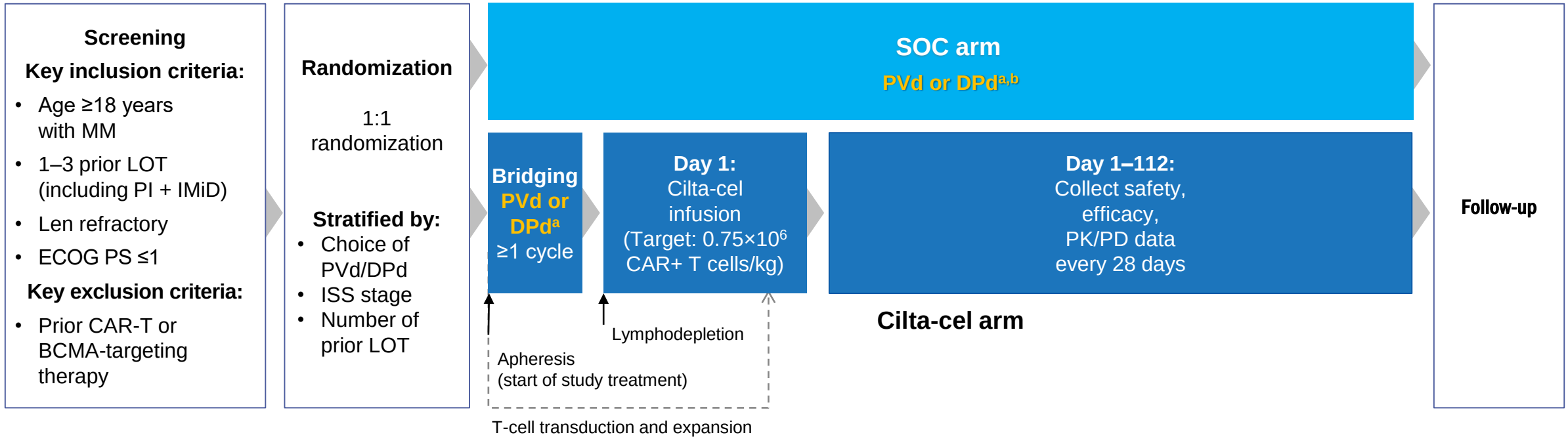
CARTITUDE-4 Study Design and Endpoints



Primary endpoint

- PFS[c]

Secondary endpoints

- Efficacy: ≥CR, ORR, MRD negativity, OS
- Safety
- PROs

[a]Physicians' choice. [b]Administered until disease progression. [c]Time from randomization to disease progression/death.
BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; cilta-cel, ciltacabtagene autoleucel; CR, complete response; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; ISS, International Staging System; Len, lenalidomide; LOT, line of therapy; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, pharmacodynamics; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; PRO, patient-reported outcome; PVd, pomalidomide, bortezomib, and dexamethasone; SOC, standard of care.

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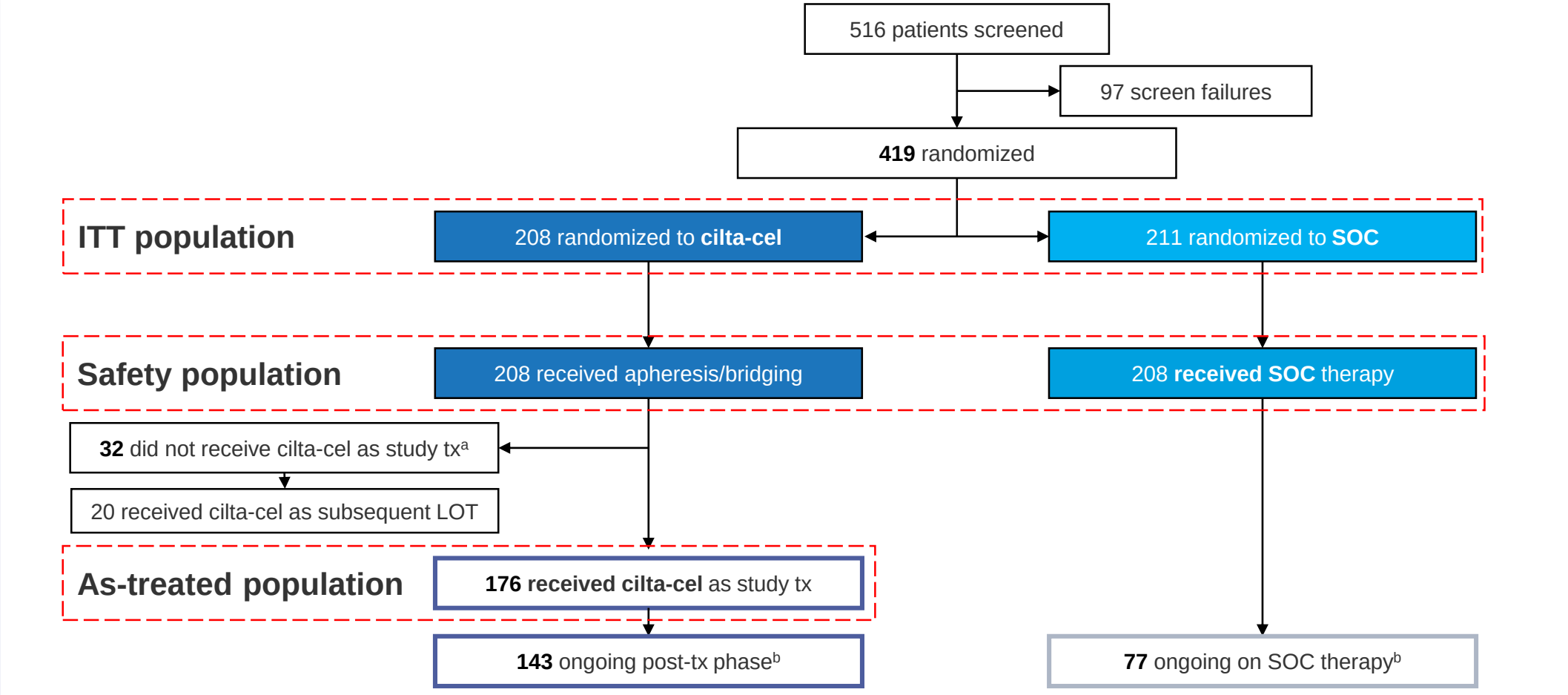
CARTITUDE-4: Patient Population and Follow-Up



- At November 1, 2022 data cut-off, median follow-up was 15.9 months (range, 0.1–27)
- First patient randomized on July 10, 2020 and last patient randomized on November 17, 2021
- Median time from first apheresis to cilta-cel infusion was 79 days

[a]Due to disease progression (n=30) or death (n=2) during bridging therapy/lymphodepletion. [b]Have not progressed.
cilta-cel, ciltacabtagene autoleucel; ITT, intent-to-treat; LOT, line of therapy; SOC, standard of care; tx, treatment.

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CARTITUDE-4 : Baseline Demographics and Disease Characteristics

Baseline characteristic	ITT population	
	Cilta-cel (n=208)	SOC (n=211)
Age, median (range), years	61.5 (27–78)	61.0 (35–80)
Male, n (%)	116 (55.8)	124 (58.8)
White, n (%)	157 (75.5)	157 (74.4)
ECOG PS ≤1, n (%) [a,b]	207 (99.5)	210 (99.5)
ISS stage, n (%)		
I	136 (65.4)	132 (62.6)
II	60 (28.8)	65 (30.8)
III	12 (5.8)	14 (6.6)
Bone marrow plasma cells ≥60%,[c] n (%)	42 (20.4)	43 (20.7)
Presence of soft tissue plasmacytomas,[d] n (%)	44 (21.2)	35 (16.6)
Years since diagnosis, median (range)	3 (0.3–18.1)	3.4 (0.4–22.1)
Prior LOT, median (range)	2 (1–3)	2 (1–3)
1 prior LOT, n (%)	68 (32.7)	68 (32.2)
2 or 3 prior LOT, n (%)	140 (67.3)	143 (67.8)

Baseline characteristic	ITT population	
	Cilta-cel (n=208)	SOC (n=211)
Cytogenetic high risk, n (%)[e]	123 (59.4)	132 (62.9)
del(17p)	49 (23.7)	43 (20.5)
t(14;16)	3 (1.4)	7 (3.3)
t(4;14)	30 (14.5)	30 (14.3)
gain/amp(1q)	89 (43.0)	107 (51.0)
2 or more high-risk cytogenetic features	43 (20.7)	49 (23.2)
del(17p), t(14;16), or t(4;14)	73 (35.3)	69 (32.9)
Triple-class[f] exposed, n (%)	53 (25.5)	55 (26.1)
Penta-drug[g] exposed, n (%)	14 (6.7)	10 (4.7)
Refractory status, n (%)		
Triple-class refractory[f,h]	30 (14.4)	33 (15.6)
Bortezomib	55 (26.4)	48 (22.7)
Pomalidomide	8 (3.8)	9 (4.3)
Daratumumab	48 (23.1)	45 (21.3)
Any PI	103 (49.5)	96 (45.5)

[a]1 patient in each arm had ECOG PS of 2. [b]Latest nonmissing ECOG PS score on or prior to apheresis/cycle 1 day 1 is used. [c]In 206 (cilta-cel arm) and 208 (SOC arm) patients, maximum value from bone marrow biopsy and bone marrow aspirate is selected if both results are available. [d]Including extramedullary and bone-based plasmacytomas with measurable soft tissue component. [e]In 207 (cilta-cel arm) and 210 (SOC arm) patients. [f]Including 1 PI, 1 IMiD, and 1 anti-CD38 monoclonal antibody. [g]Including ≥2 PI, ≥2 IMiDs, and 1 anti-CD38 monoclonal antibody. [h]2 patients (cilta-cel arm) and 1 patient (SOC arm) were penta-drug refractory, including ≥2 PI, ≥2 IMiDs, and 1 anti-CD38 monoclonal antibody.

cilta-cel, ciltacabtagene autoleucel; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; ITT, intent-to-treat; LOT, line of therapy; PI, proteasome inhibitor; SOC, standard of care.

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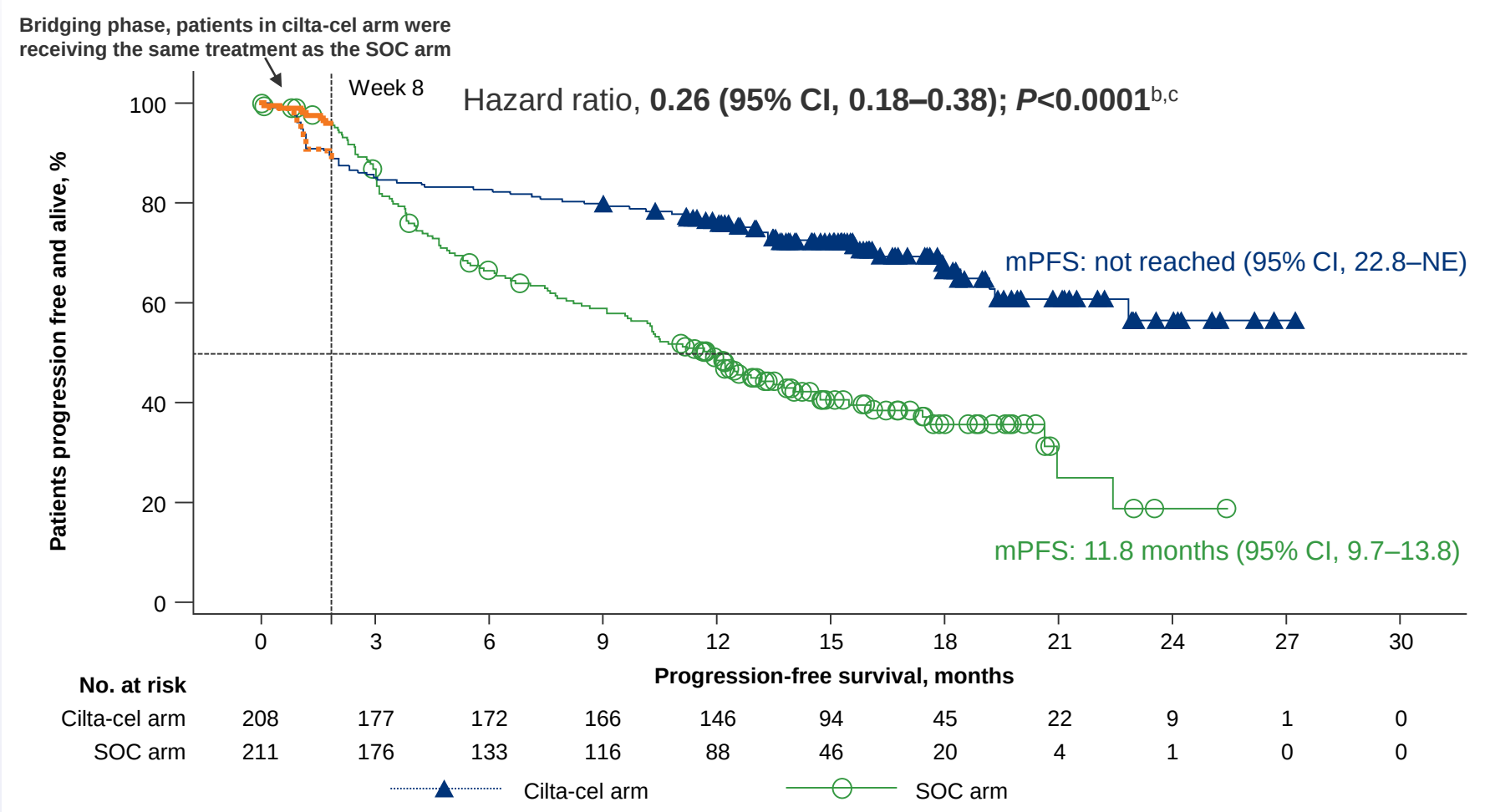
CARTITUDE-4:Primary Endpoint – PFS (ITT Population)

Cilta-cel vs SOC

- 12-month PFS rate: 76% vs 49%
- SOC performed as expected



[a]Median follow-up, 15.9 months. [b]Constant piecewise weighted log-rank test. [c]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.
cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; ITT, intent-to-treat; mPFS, median progression-free survival; NE, not estimable; SOC, standard of care.

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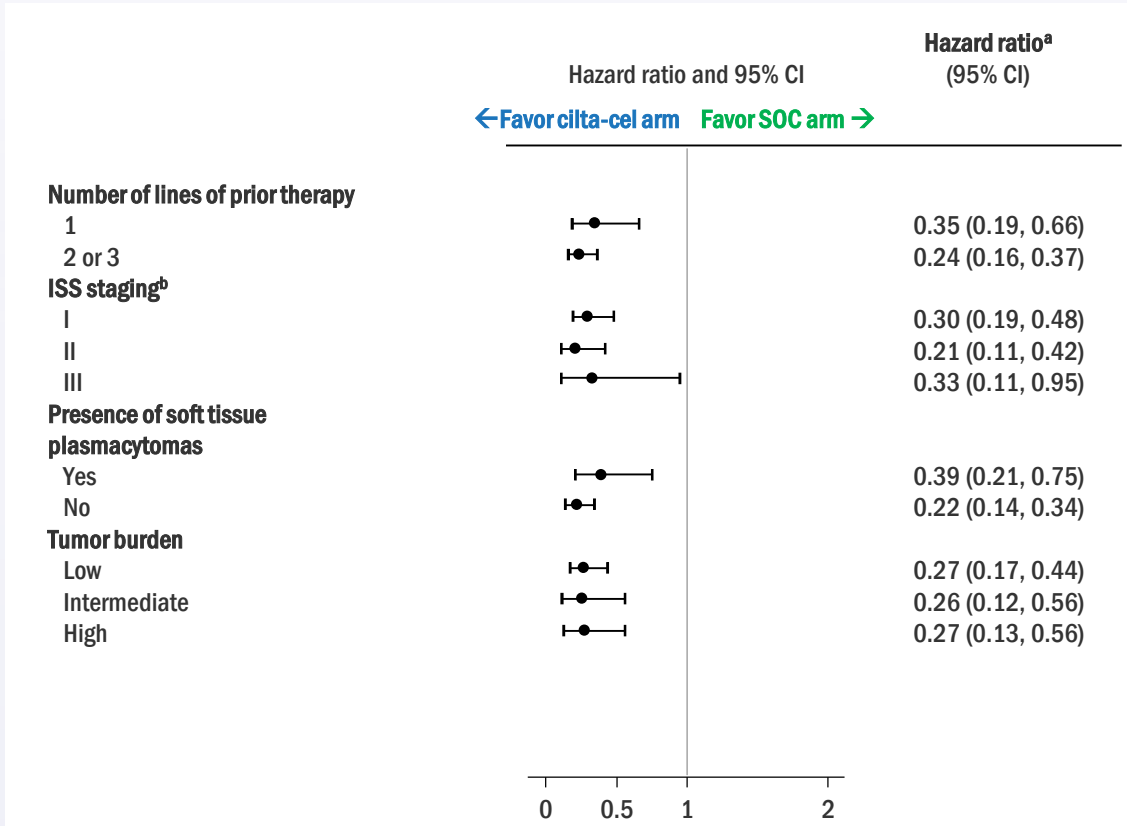
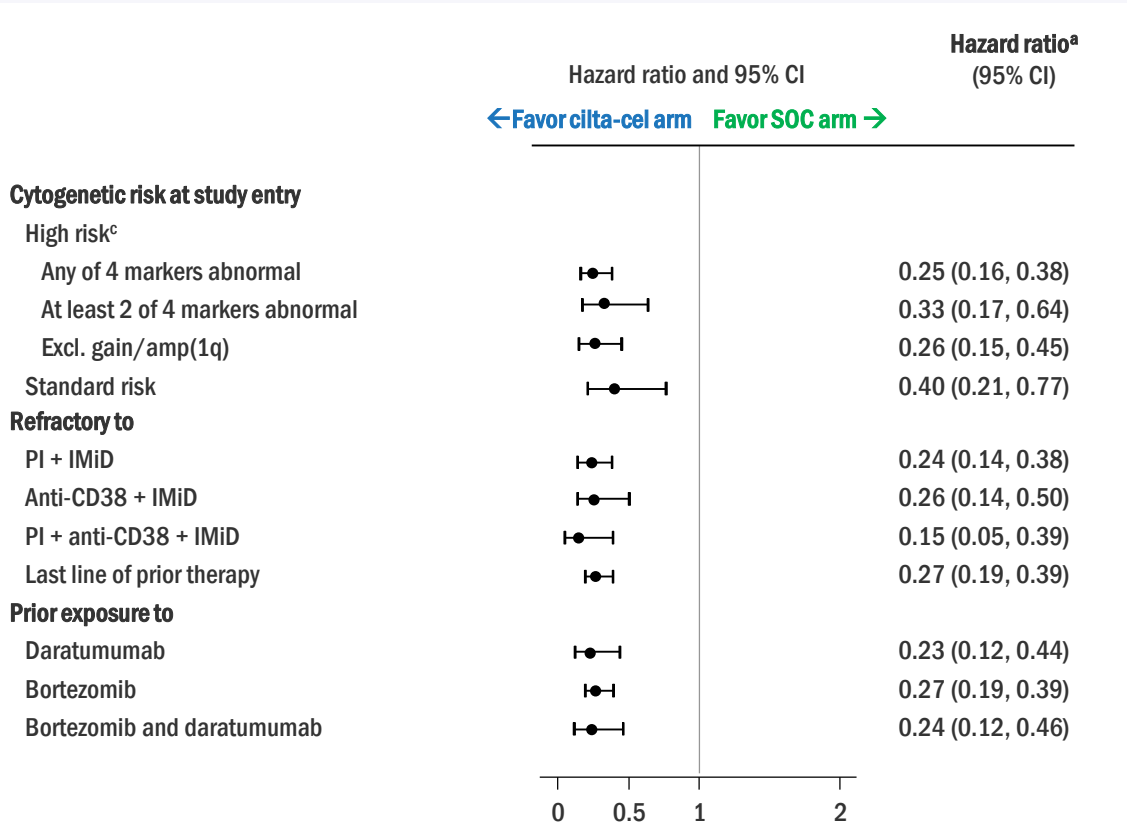
CARTITUDE-4: Key Subgroup Analysis (ITT)





[a]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. A hazard ratio <1 indicates an advantage for the cilta-cel arm. [b]Based on serum β_2-microglobulin and albumin. [c]Positive for del(17p), t(14;16), t(4;14), and/or gain/amp(1q) by fluorescence in situ hybridization testing. Protocol-defined high-risk cytogenetics refers to "Any of 4 markers abnormal."

cilta-cel, ciltacabtagene autoleucel; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; ISS, International Staging System; PI, proteasome inhibitor; SOC, standard of care.

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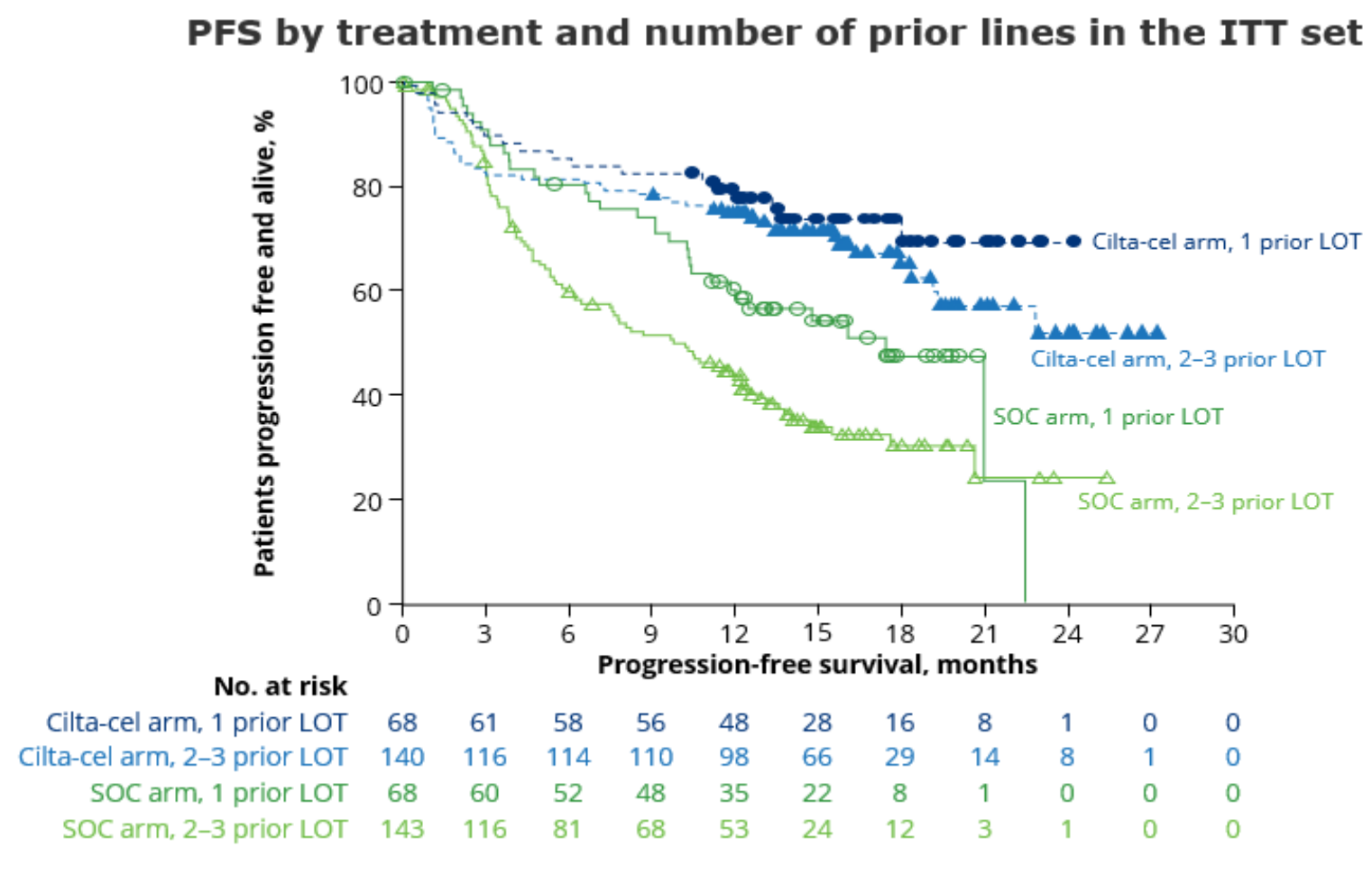
CARTITUDE-4: PFS by Prior Line of Therapy

- Cilta-cel improved PFS vs SOC whether patients had 1 or 2–3 prior LOT



cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; ITT, intent-to-treat; LOT, line of therapy; PFS, progression-free survival; SOC, standard of care.

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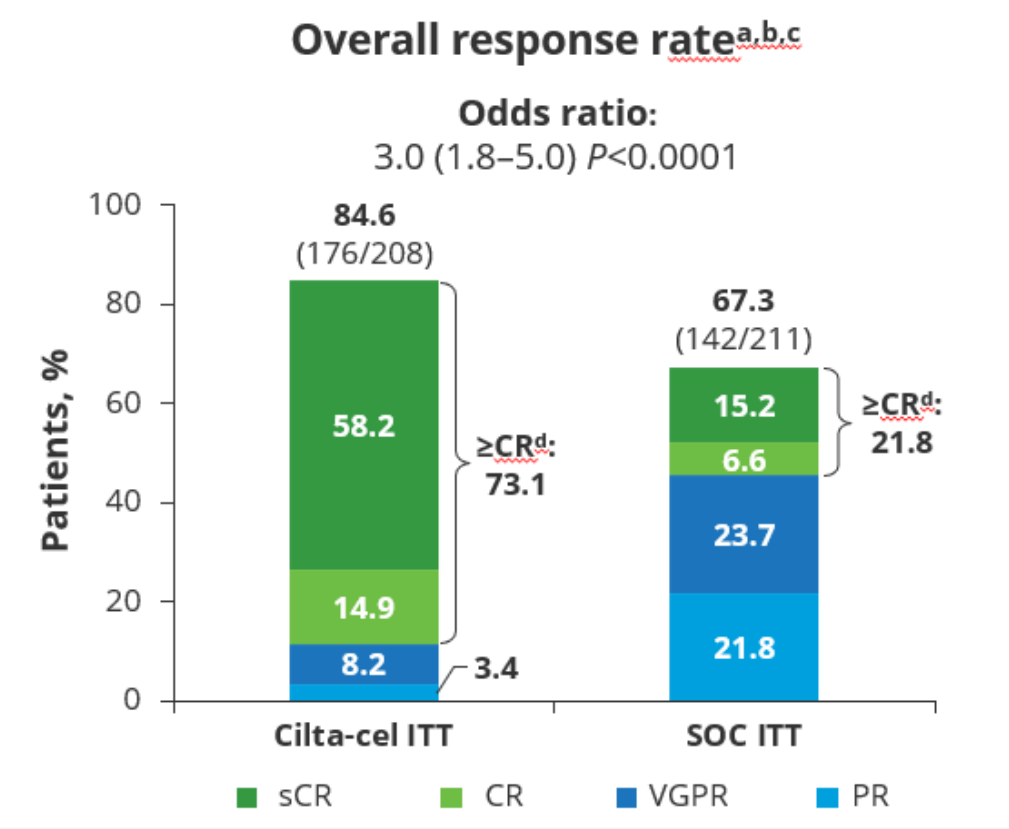
CARTITUDE-4: Secondary Endpoint (ITT) – Response

Cilta-cel had higher ORR vs SOC



Outcome	Cilta-cel (N=208)	SOC (N=211)
12-month DOR rate, % (95% CI)	84.7 (78.1–89.4)	63.0 (54.2–70.6)
Duration of response, months median (95% CI)	NR	16.6 (12.9–NE)

[a]Assessed using a validated computerized algorithm; ORR is defined as the proportion of subjects who achieve a PR or better per IMWG criteria. [b]*P*-value from the Cochran Mantel-Haenszel Chi-Squared test. [c]In 176 patients who received cilta-cel as study treatment, ORR was 99%, ≥CR rate was 86%.[d]Odds ratio, 10.3; *P*<0.0001.

CR, complete response; DOR, duration of response; IMWG, International Myeloma Working Group; ITT, intent-to-treat; NE, not estimable; NR, not reached; ORR, overall response rate; PR, partial response; sCR, stringent complete response; SOC standard of care; VGPR, very good partial response.

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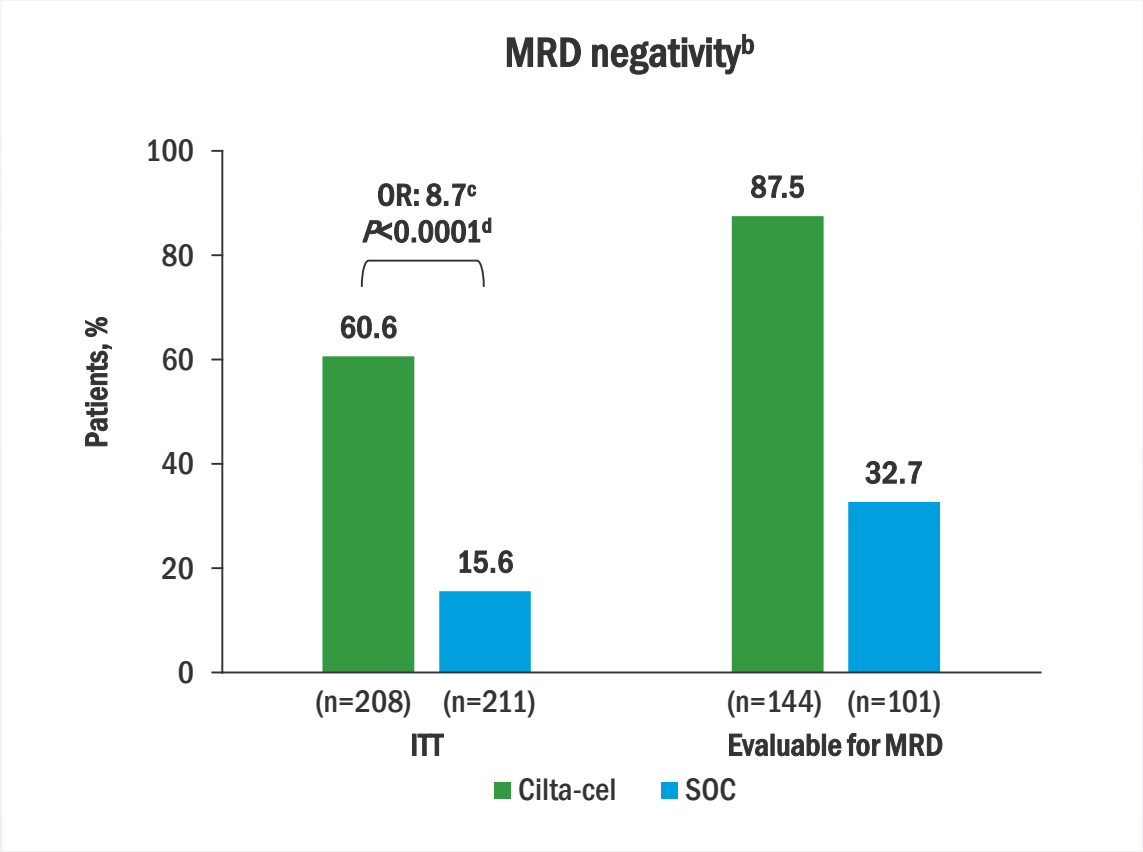
CARTITUDE-4: Secondary Endpoints – MRD and OS

Cilta-cel improved rates of overall MRD negativity[a,b] at 10^{-5} vs SOC



OS was immature with 39 deaths in cilta-cel arm vs 47[e] deaths in SOC arm:

- HR, 0.78; 95% CI, 0.5–1.2, *P*=0.26

[a]Assessed by next-generation sequencing. [b]Achieved at any time during the study up to data cut-off. [c]Stratified Cochran Mantel-Haenszel test. [d]Fisher's Exact Test; [e]1 patient in the SOC arm died prior to initiation of treatment and was not included in the safety set; in the safety population (SOC arm), there were 46 deaths.
cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; ITT, intent-to-treat; MRD, minimal residual disease; OS, overall survival; SOC standard of care.

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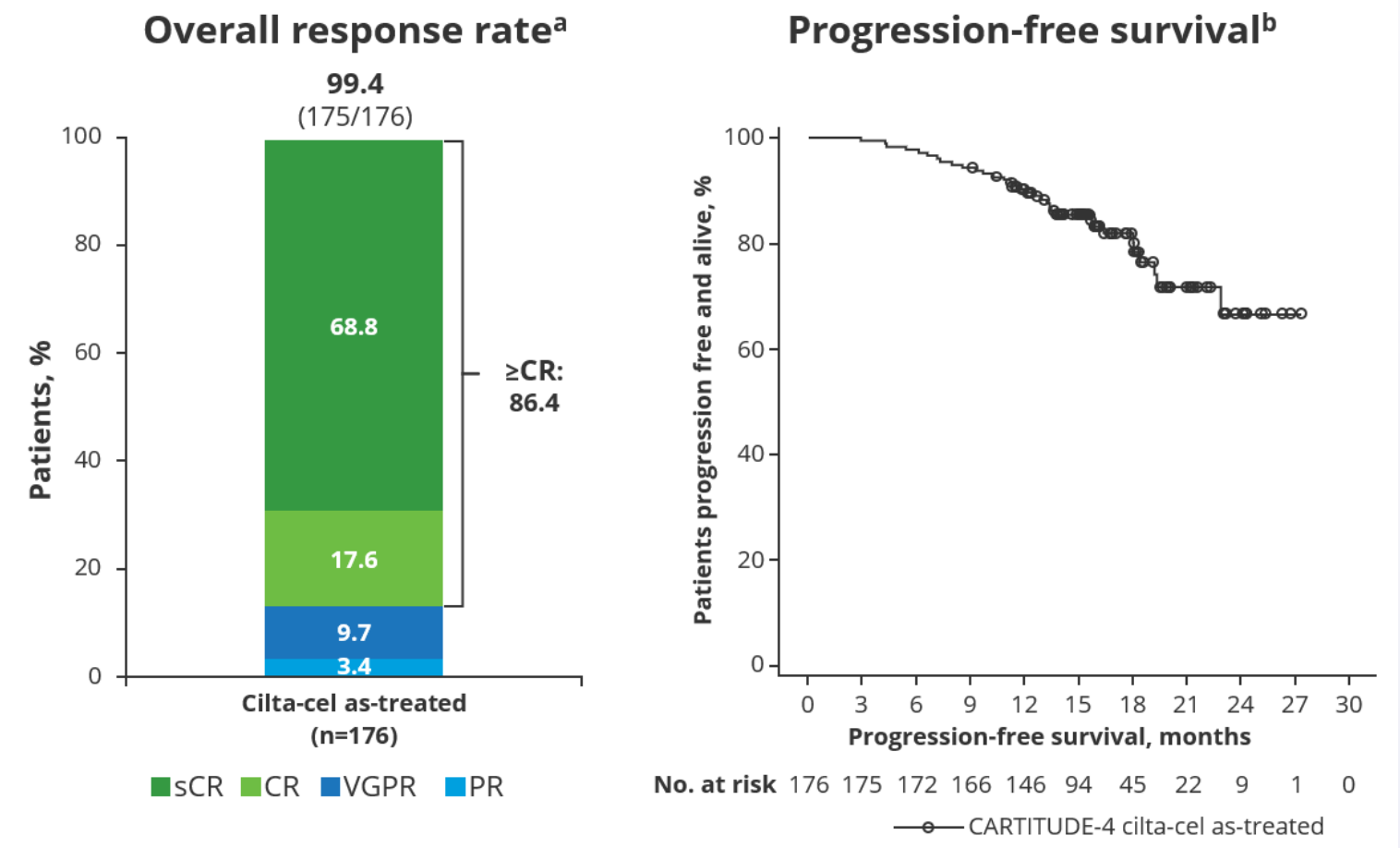
CARTITUDE-4: Patients Treated With Cilta-cel as Study Treatment (As-Treated Population)



- For the as-treated population (n=176):
  - 99% ORR, with 86% ≥CR
  - 72% MRD negative at 10^{-5} (n=126/176)
  - 90% PFS rate (from apheresis) at 12 months

[a]Assessed using a validated computerized algorithm; ORR is defined as the proportion of subjects who achieve a PR or better per IMWG criteria. [b]Baseline begins at apheresis and excludes patients randomized to cilta-cel who had disease progression during bridging therapy or lymphodepletion, or died, and thus were not eligible to receive cilta-cel as study treatment.
cilta-cel, ciltacabtagene autoleucel; CR, complete response; IMWG, International Myeloma Working Group; ORR, overall response rate; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; SOC standard of care; VGPR, very good partial response.

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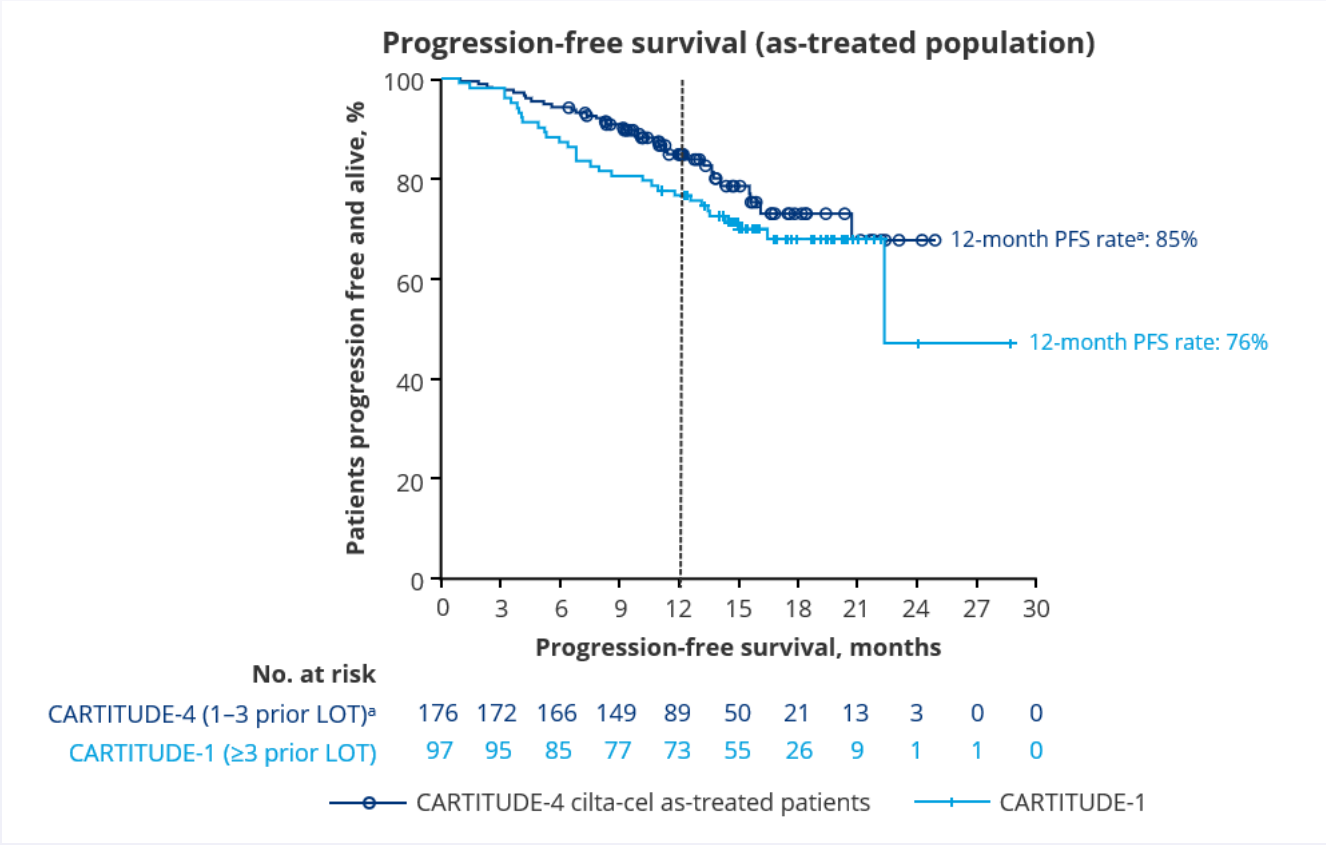
CARTITUDE-4: PFS Versus CARTITUDE-1

Rate of PFS in CARTITUDE-4 numerically better than in 18-month follow-up of CARTITUDE-1[1]



Outcome, %	CARTITUDE-4 16-month median follow-up	CARTITUDE-1[1] 18-month median follow-up
12-month PFS rate (from cilta-cel infusion)	85[a]	76
≥CR or better rate	86	80
MRD negativity rate[b] (10^{-5})	72	58

[a]Re-baselined to begin at time of cilta-cel infusion for patients who received cilta-cel as study treatment, with median follow-up of 13 months. [b]For all patients who received cilta-cel as study treatment in CARTITUDE-4 (n=176) and all patients (n=97) in CARTITUDE-1.
cilta-cel, ciltacabtagene autoleucel; CR, complete response; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival.
[1]Usmani SZ, et al. *J Clin Oncol* 2021;39:15_suppl, 8005.

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CARTITUDE-4: TEAEs

Select TEAE ≥15%, n (%)	Safety population			
	Cilta-cel (n=208)		SOC (n=208)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any AE	208 (100)	201 (96.6)	208 (100)	196 (94.2)
Serious AE	92 (44.2)	67 (32.2)	81 (38.9)	70 (33.7)
Hematologic	197 (94.7)	196 (94.2)	185 (88.9)	179 (86.1)
Neutropenia	187 (89.9)	187 (89.9)	177 (85.1)	172 (82.2)
Anemia	113 (54.3)	74 (35.6)	54 (26.0)	30 (14.4)
Thrombocytopenia	113 (54.3)	86 (41.3)	65 (31.3)	39 (18.8)
Lymphopenia	46 (22.1)	43 (20.7)	29 (13.9)	25 (12.0)
Infections	129 (62.0)	56 (26.9)	148 (71.2)	51 (24.5)
Upper respiratory tract[a]	39 (18.8)	4 (1.9)	54 (26.0)	4 (1.9)
Lower respiratory tract[b]	19 (9.1)	9 (4.3)	36 (17.3)	8 (3.8)
COVID-19[c]	29 (13.9)	6 (2.9)	55 (26.4)	12 (5.8)

- **Hematologic TEAEs most common**
  - 85–90% **neutropenia**, almost all grade 3/4
  - Most high-grade cytopenias **resolved to grade ≤2 by day 30**
  - Grade 3/4 infections similar between arms
- **Second primary malignancies:**
  - Cilta-cel, 4.3% (n=9); most commonly cutaneous/noninvasive and hematologic
  - SOC, 6.7% (n=14); most commonly cutaneous/noninvasive[d]
- **Deaths due to TEAEs**
  - Cilta-cel, n=10[e] (7 due to COVID-19[f])
  - SOC, n=5[g] (1 due to COVID-19)

[a]Includes preferred terms upper respiratory tract infection, nasopharyngitis, sinusitis, rhinitis, tonsillitis, pharyngitis, laryngitis, and pharyngotonsillitis. [b]Includes preferred terms lower respiratory tract infection, pneumonia, and bronchitis. [c]Treatment-emergent COVID-19 only; includes preferred terms COVID-19, COVID-19 pneumonia, and asymptomatic COVID-19. [d]With 1 case of peripheral T-cell lymphoma in the cilta-cel arm. [e]7 due to COVID-19, and 1 each due to neutropenic sepsis, pneumonia, and respiratory failure. [f]3 of 7 who died from COVID-19 were unvaccinated prior to cilta-cel. These COVID-19–related deaths contributed to the higher number of fatal events in the first year. [g]1each due to COVID-19, progressive multifocal leukoencephalopathy, respiratory tract infection, septic shock, and pulmonary embolism.
AE, adverse event; cilta-cel, ciltacabtagene autoleucel; TEAE, treatment-emergent adverse event; SOC, standard of care.

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LEGEND BIOTECH

CARTITUDE-4: CRS and CAR-T Cell-Related Neurotoxicity

AEs, n (%)	As-treated patients (n=176)				
	Any grade	Grade 3/4	Median time to onset, days	Median duration, days	Resolved, n
CRS	134 (76.1)	2 (1.1)	8	3	134
Neurotoxicity[a]	36 (20.5)	5 (2.8)			
ICANS	8 (4.5)	0[b]	10	2	8
Other[c]	30 (17.0)	4 (2.3)			
Cranial nerve palsy[d]	16 (9.1)	2 (1.1)	21	77	14
Peripheral neuropathy	5 (2.8)	1 (0.6)	63	201	3
MNT	1 (0.6)	0	85	–	0

In the cilta-cel as-treated population:

- 30 patients had non-ICANS neurotoxicities[c]
  - 16 cranial nerve palsies (14 recovered)
  - 5 peripheral neuropathies
  - 1 MNT (grade 1)
- **Lower incidence and severity of CRS, ICANS, MNTs, and some cytopenias[e] observed with CARTITUDE-4 vs CARTITUDE-1**
  - Cilta-cel may be better tolerated when used earlier in treatment
  - Effective bridging therapy enables better control of tumor burden prior to CAR-T infusion
  - MNTs were lower likely related to patient management strategies implemented to mitigate this risk

[a]There were no fatal neurotoxicities. [b]Grade 3 syncope reported as a symptom of grade 2 ICANS. [c]Other neurotoxicities include AEs reported as CAR-T cell neurotoxicity that are not ICANS or associated symptoms. [d]Cranial nerve palsies most commonly affected cranial nerve VII; supportive measures included corticosteroids (14 patients). No clear risk factors for cranial nerve palsies have been identified, and the mechanism is not understood. [e]Data for cytopenias not shown.
AE, adverse event; CAR-T, chimeric antigen receptor T cell; cilta-cel, ciltacabtagene autoleucel; CRS, cytokine release syndrome; DPd, daratumumab, pomalidomide, and dexamethasone; ICANS, immune effector cell–associated neurotoxicity syndrome; MNT, movement and neurocognitive treatment-emergent adverse event.

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CARTITUDE-4: Conclusions

- **Cilta-cel significantly prolonged PFS vs SOC** (HR, 0.26; *P*<0.0001) in patients with lenalidomide-refractory MM and 1–3 prior LOT
  - **PFS benefit was seen across all subgroups**, including patients with high-risk cytogenetics (including in patients with 2 or more high-risk features), soft tissue plasmacytomas, ISS stage III disease, and prior exposure to anti-CD38 antibodies and PI
- Cilta-cel significantly increased ORR and depth of response vs SOC
  - ORR in the cilta-cel as-treated group was 99%, with 86% ≥CR and 72% MRD negative (10^{-5})
- **CAR-T–specific AEs were manageable** with appropriate supportive care
- Lower incidence and severity of CRS, ICANS, MNT, and some cytopenias were observed in CARTITUDE-4 vs CARTITUDE-1,[1,2] suggesting **improved tolerability of cilta-cel when used earlier in treatment**

If approved, cilta-cel has the potential to be a new standard of care for patients with lenalidomide-refractory myeloma after first relapse

AE, adverse event; CAR-T, chimeric antigen receptor T cell; cilta-cel, ciltacabtagene autoleucel; CR, complete response; CRS, cytokine release syndrome; HR, hazard ratio; ICANS, immune effector cell–associated neurotoxicity syndrome; ISS, International Staging System; LOT, line of therapy; MM, multiple myeloma; MNT, movement and neurocognitive treatment-emergent adverse event; MRD, minimal residual disease; ORR, overall response rate; PFS, progression-free survival; PI, proteasome inhibitor; sCR, stringent complete response; SOC, standard of care.

1. Usmani SZ, et al. *J Clin Oncol* 2021;39:15_suppl, 8005. 2. Martin T, et al. *J Clin Oncol* 2023;41:1265-74.

Dhakal et al. ASCO Annual Meeting; June 2-6, 2023; Chicago, Il & Virtual; Abstract #LBA106

CARTITUDE-1

End of Study Results (~3-year Follow-up)
Primary Efficacy and Safety

CARTITUDE-1 Final Results: Introduction
(~3-Year Follow-Up)

- Ciltacabtagene autoleucel (cilta-cel) is a dual-binding, BCMA, CAR-T cell therapy for the treatment of patients with RRMM[1,2]
  - Heavily pretreated patients with RRMM who are treated with standard-of-care therapy have a median OS of ~9–12 months[3,4]
- In the single-arm, phase 1b/2 CARTITUDE-1 study (NCT03548207), a single cilta-cel infusion induced early, deep, and durable responses in heavily treated patients with RRMM[1,2]
  - At median follow-up of 27.7 months, median DOR, PFS, and OS were not reached[2]
  - 27-month rates of PFS and OS were 54.9% and 70.4%, respectively[2]
- Cilta-cel was approved for the treatment of adult patients with RRMM after ≥4 (in the United States) or ≥3 (in Europe) prior LOT, including an IMiD, a PI, and an anti-CD38 mAb[5,6]

Objective: To report study closeout results from CARTITUDE-1 at a median follow-up of 33.4 months

CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; BCMA, B-cell maturation antigen; DOR, duration of response; IMiD, immunomodulatory drug; LOT, line of therapy; mAb, monoclonal antibody; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma.

1. Berdeja JG, et al. *Lancet* 2021;398:314-24. 2. Martin T, et al. *J Clin Oncol* 2023;41:1265-74. 3. Mateos M-V, et al. *Leukemia* 2022;36:1371-6. 4. Gandhi UH, et al. *Leukemia* 2019;33:2266-75. 5. CARVYKTI (ciltacabtagene autoleucel). Package insert. Janssen Biotech, Inc.; 2023. 6. CARVYKTI® (ciltacabtagene autoleucel). European Medicines Agency. Orphan maintenance assessment report. June 7, 2022. Accessed March 23, 2023. https://www.ema.europa.eu/en/documents/orphan-maintenance-report/carvykti-orphan-maintenance-assessment-report-initial-authorisation_en.pdf.

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LEGEND BIOTECH

CARTITUDE-1 Final Results: Study Population and Endpoints
(~3-Year Follow-Up)

Study population

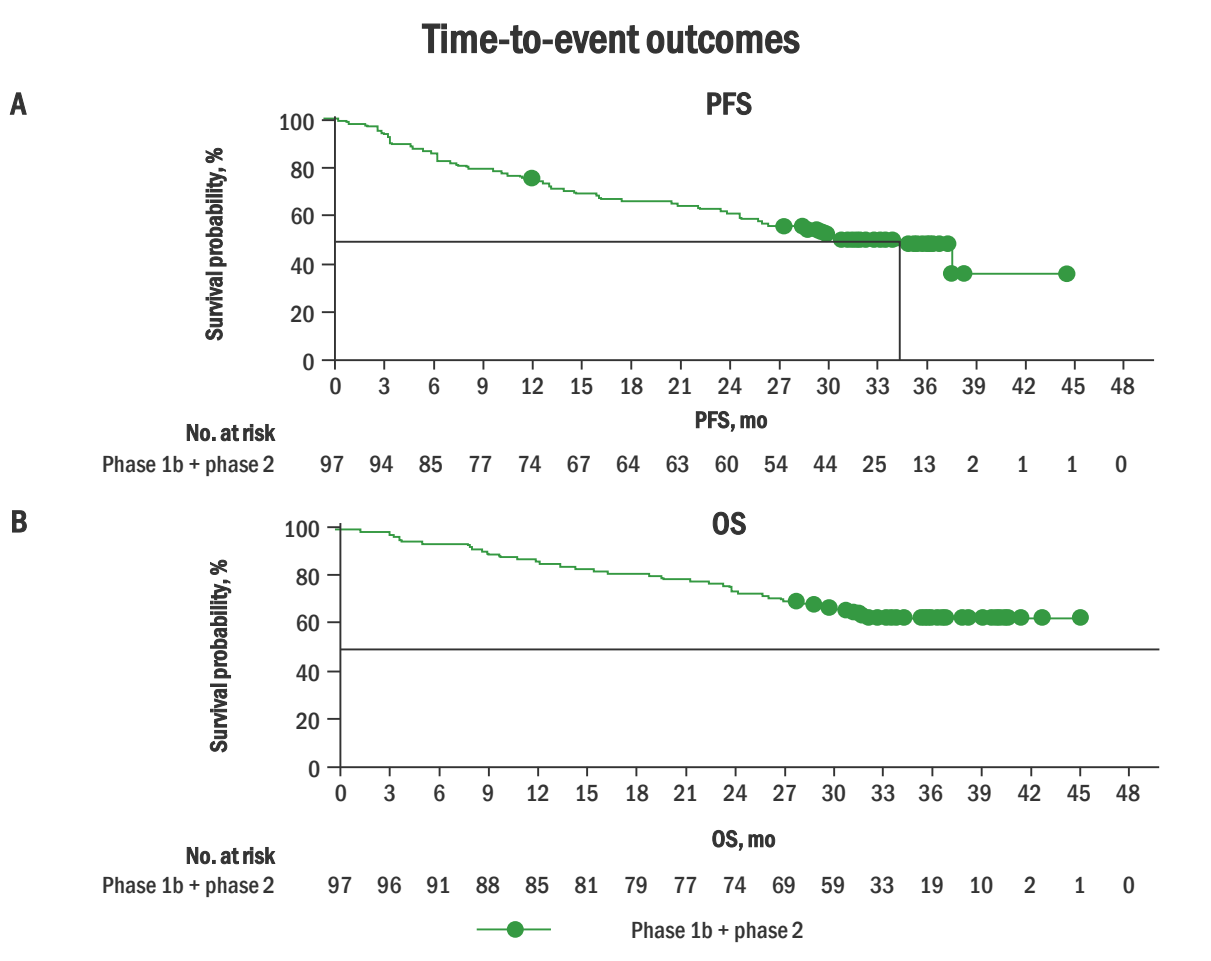
- As of October 14, 2022, 97 patients were treated with cilta-cel, with a median follow-up of 33.4 months (range, 1.5–45.2)
- Patient demographics and baseline characteristics have been previously described[1,2]

Previously reported primary endpoint

- ORR as assessed by independent review committee was 97.9% (95% CI, 92.7–99.7), and 82.5% (95% CI, 73.4–89.4) of patients achieved sCR[2]

At study closeout:

- Median DOR was 33.9 months (95% CI, 25.5–NE)
- Median PFS was 34.9 months (95% CI, 25.2–NE)
- Median OS was not reached



cilta-cel, ciltacabtagene autoleucel; DOR, duration of response; NE, not estimable; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; sCR, stringent complete response.

1. Berdeja JG, et al. *Lancet* 2021;398:314-24. 2. Martin T, et al. *J Clin Oncol* 2023;41:1265-74.

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CARTITUDE-1 Final Results: MRD Results
(~3-Year Follow-Up)

- 62 patients had samples evaluable for MRD at any time, and 49 patients had samples evaluable for 12-month sustained MRD
  - Of these 49 evaluable patients, 26 had sustained MRD negativity for ≥12 months
    - Of the 26 patients, 20 had sustained MRD-negative ≥CR
- At 24 months post cilta-cel infusion, 18 patients remained MRD negative with ≥CR

PFS by CR and sustained MRD negativity

Subgroups	mPFS (95% CI), mo	30-mo PFS rate	36-mo PFS rate
All patients	34.9 (25.2–NE)	54.2%	47.5%
≥CR[a]	38.2 (34.9–NE)	66.8%	59.8%
12-mo sustained MRD negativity[b]	NR (NE–NE)	74.9%	NE
12-mo sustained MRD-negative ≥CR[b]	NR (NE–NE)	78.5%	NE

[a]Patients had ≥CR at any time during the study, assessed by computerized algorithm. [b]Patients who were MRD evaluable had a baseline clone identified, sufficient follow-up for assessment, ≥2 MRD-negative assessments 12 mo apart, with no MRD-positive samples in that interval.
cilta-cel, ciltacabtagene autoleucel; CR, complete response; mPFS, median progression-free survival; MRD, minimal residual disease; NE, not estimable, NR, not reached; PFS, progression-free survival.

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CARTITUDE-1 Final Results: Safety
(~3-Year Follow-Up)

- No new neurotoxicity events were reported since the 27.7-month median follow-up[1]
- A total of 26 SPMs were reported in 20 patients
  - 4 new patients developed SPMs since 27.7-month median follow-up, with 6 newly reported cases
- A total of 35 deaths occurred
  - 5 new deaths unrelated to cilta-cel were reported since the 27.7-month median follow-up:
    - Progressive disease (n=3)
    - Pneumonia (n=1)
    - Sepsis (n=1)

TABLE: Study deaths

	Patients (N=97)	Time of death post cilta-cel infusion, days
Total deaths during the study	35	45–980
Due to progressive disease	17	253–980
AEs unrelated to treatment	**12**	
Pneumonia	2	109; 887
AML[a]	3	418; 582; 718
Ascites[b]	1	445
MDS	1	803
Respiratory failure	3	733; 793; 829
Septic shock and/or sepsis	2	917; 945
AEs related to treatment	**6**	
Septic shock and/or sepsis	2	45; 162
CRS/HLH	1	99
Lung abscess	1	119
Respiratory failure	1	121
Neurotoxicity	1	247

[a]One patient with AML also had MDS and a cytogenetic profile consistent with MDS (del(20q) [present before cilta-cel infusion], loss of 5q); another patient who died from AML had both prostate cancer and squamous cell carcinoma of the scalp. [b]Patient died from ascites (unrelated to cilta-cel as assessed by the investigator) due to noncirrhotic portal fibrosis and nonalcoholic steatosis that was present for many years preceding the study.
AML, acute myelogenous leukemia; AE, adverse event; cilta-cel, ciltacabtagene autoleucel; CRS, cytokine release syndrome; HLH, hemophagocytic lymphohistiocytosis; MDS, myelodysplastic syndrome; SPM, second primary malignancy.

1. Martin T, et al. *J Clin Oncol* 2023;41:1265-74.

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CARTITUDE-1 Final Results: Conclusions
(~3-Year Follow-Up)

- At 3-year follow-up:
  - An estimated 62.9% of patients were alive
  - There were no new neurotoxicity events
- Achieving CR and/or sustained MRD negativity was associated with prolonged PFS
- Patients continue to be followed for safety and survival in the 15-year CARTINUE long-term study (NCT05201781; MMY4002)[1]

At CARTITUDE-1 study closeout, a single infusion of cilta-cel provided a median PFS of 34.9 months; cilta-cel is the only FDA / EMA approved therapy to display a benefit of this magnitude for patients in this setting in clinical trials

BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; CR, complete response; MRD, minimal residual disease; PFS, progression-free survival.

1. ClinicalTrials.gov. CARTINUE (NCT05201781).

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LEGEND-2

≥5-Year Follow-Up

LEGEND-2 5-Year Results: Introduction

- LCAR-B38M CAR T cells express a structurally differentiated CAR construct containing a 4-1BB costimulatory domain and 2 BCMA-targeting, single-domain antibodies to confer avidity[1]
- LEGEND-2 was a first-in-human phase 1 study of LCAR-B38M conducted at 4 sites in China,[2,3] which showed encouraging efficacy and manageable safety in 74 patients with RRMM[3]
  - At median follow-up of 48 months, the ORR was 87.8%, and 73.0% patients achieved CR[3]
  - Median PFS was 18.0 months, median OS was not reached, and median DOR was 23.3 months[3]
- The efficacy observed in LEGEND-2 was confirmed by the US phase 1b/2 CARTITUDE-1[4,5] and Chinese phase 2 CARTIFAN-1[6] studies of ciltacabtagene autoleucel, which expresses the same CAR as LCAR-B38M

Objective: To report ≥5-year follow-up data from LEGEND-2, the longest follow-up for any BCMA-targeted CAR-T cell therapy

CAR, chimeric antigen receptor; CR, complete response; DOR, duration of response; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma.

1. Xu J, et al. *PNAS* 2019;116:9543-51. 2. Zhao W-H, et al. *J Hematol Oncol* 2018;11:141. 3. Zhao W-H, et al. *J Hematol Oncol* 2022;15:86. 4. Berdeja JG, et al. *Lancet* 2021;398:314-24. 5. Martin T, et al. *J Clin Oncol* 2023;41:1265-74. 6. Mi J-Q, et al. *J Clin Oncol* 2023;41:1275-84.

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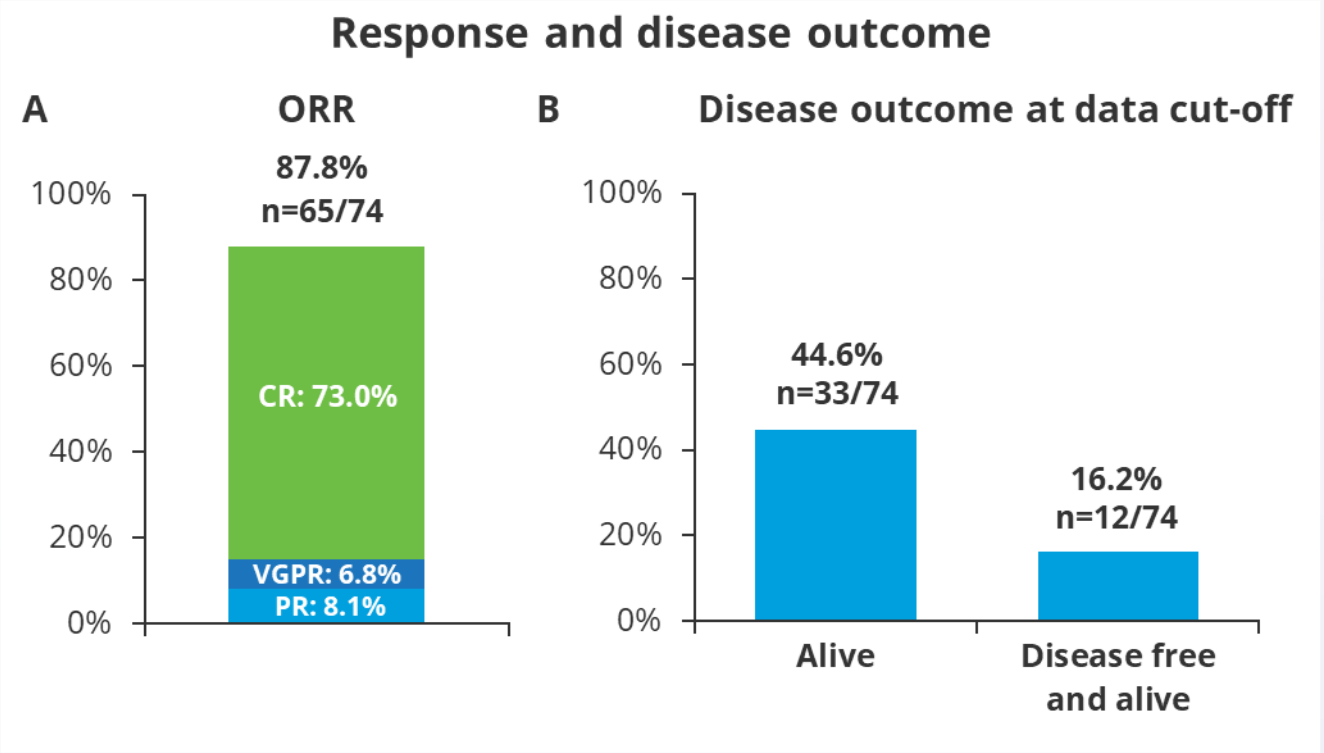
LEGEND-2 5-Year Results: Efficacy

- As of November 2022, 74 patients were treated with LCAR-B38M with a median follow-up of 65.4 months (range, 0.4–78.8), 5 years after the last patient was dosed
- ORR was mature at 87.8% (95% CI, 78.2–94.3) and unchanged since 48-month follow-up
  - Median DOR was 23.3 months (95% CI,13.0–36.5)
  - Minimal residual disease-negative CR rate (at 10-4) was 67.6%
- 33 (44.6%) patients were alive at data cut-off, of whom 12 (16.2%) were disease free ≥5 years after infusion, suggesting functional cure in these patients



CR, complete response; DOR, duration of response; ORR, overall response rate; PR, partial response; VGPR, very good partial response.

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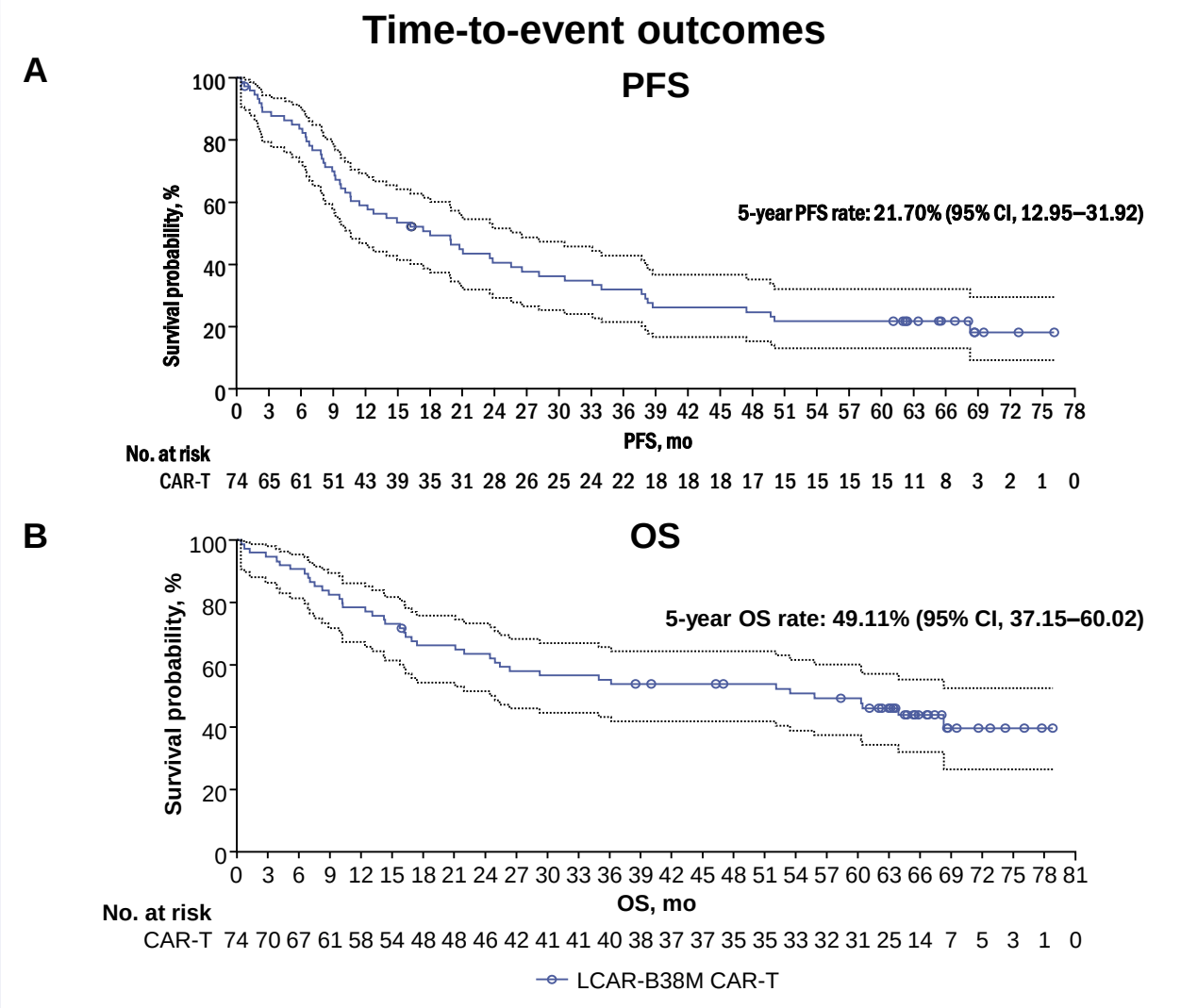
LEGEND-2 5-Year Results: Efficacy (cont'd)

- Median PFS was 18.0 months (95% CI, 10.6–26.6)
- Median OS was reached with this data cut and was 55.8 months (95% CI, 24.4–not evaluable)
- Compared with patients who were progression free, patients who progressed or died had higher-risk features at baseline, including longer time from diagnosis, more prior LOT, baseline ECOG PS 1 or 2, ISS stage II or III, less IgG-type MM, more light-chain MM, and presence of EMD
- No new CAR-T cell–related toxicities were reported since 48-month follow-up; the incidence of neurotoxicity was 1%[1]



CAR-T, chimeric antigen receptor T cell; PFS; progression free survival; OS, overall survival.

1. Zhao W-H, et al. *J Hematol Oncol* 2022;15:86.

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LEGEND-2 5-Year Results: Conclusions

- At 65.4 months follow-up in LEGEND-2, 16% of patients remained disease free and alive for ≥5 years; median OS was 55.8 months, and 45% were still alive, suggesting long-term OS benefit even for patients who progressed
- No new safety signals were reported at this longer follow-up, demonstrating a favorable long-term safety profile of LCAR-B38M
- Patients who are less heavily pretreated or have good functional status may experience greater benefit with potential for cure, after LCAR-B38M CAR-T cell therapy

At ≥5-year follow-up in LEGEND-2, LCAR-B38M therapy demonstrated strong efficacy with median overall survival of 55.8 months; 16% of patients remaining disease free at a median of 65.4 months suggests the possibility of a cure for some with heavily pretreated RRMM

CAR, chimeric antigen receptor; OS, overall survival; RRMM, relapsed/refractory multiple myeloma.

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THANK YOU