Overall Survival With Ciltacabtagene Autoleucel Versus Standard of Care in Lenalidomide-Refractory Multiple Myeloma: Phase 3 CARTITUDE-4 Study Update

María-Victoria Mateos[1], Jesús San-Miguel[2], Binod Dhakal[3], Cyrille Touzeau[4], Xavier Leleu[5], Niels WCJ van de Donk[6], Surbhi Sidana[7], Albert Oriol[8], Yaël C Cohen[9], Simon J Harrison[10, 11, 12], Hermann Einsele[13], Paolo Corradini[14], Diana Chen[15], Quanlin Li[16], Katherine Li[17], Ana Slaughter[18], Carolina Lonardi[19], Nina Benachour[20], Martin Vogel[21], Nikoletta Lendvai[22], Mythili Koneru[23], Nitin Patel[23], Erika Florendo[23], P Joy Ho[24], Rakesh Popat[25]

[1]University Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain; [2]Cancer Center Clinica Universidad Navarra, CIMA, IDISNA, Pamplona, Spain; [3]Medical College of Wisconsin, Milwaukee, WI, USA; [4]Centre Hospitalier Universitaire de Nantes, Nantes, France; [5]CHU Poitiers, Poitiers, France; [6]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [7]Stanford University School of Medicine, Stanford, CA, USA; [8]Institut Català d'Oncologia and Institut Josep Carreras, Hospital Germans Trias i Pujol, Badalona, Barcelona, Spain; [9]Tel Aviv Sourasky (Ichilov) Medical Center, Faculty of Medical & Health Sciences, Tel Aviv University, Tel Aviv, Israel; [10]Peter MacCallum Cancer Centre, Melbourne and Royal Melbourne Hospital, Melbourne, Australia; [11]Translation Laboratory, Centre of Excellence in Cellular Immunotherapy, Peter MacCallum Cancer Centre, Melbourne, Australia; [12]Sir Peter MacCallum Department of Oncology, University of Melbourne, Parkville, Australia; [13]Universitätsklinikum Würzburg, Medizinische Klinik und Poliklinik II, Würzburg, Germany; [14]Fondazione IRCCS Istituto Nazionale dei Tumori Milano, University of Milano, Italy; [15]Janssen Research & Development, Shanghai, China; [16]Janssen Research & Development, Apex, NC, USA; [17]Janssen Research & Development, Spring House, PA, USA; [18]Cilag GmbH International, Zug, Switzerland; [19]Janssen, Buenos Aires, Argentina; [20]Janssen Research & Development, Beerse, Belgium; [21]Janssen Research & Development, Neuss, Germany; [22]Janssen Research & Development, Raritan, NJ, USA; [23]Legend Biotech USA Inc., Somerset, NJ, USA; [24]Royal Prince Alfred Hospital and University of Sydney, Sydney, Australia; [25]University College London Hospitals, NHS Foundation Trust, London, UK

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Disclosures

- María-Victoria Mateos has received honoraria from AbbVie, Amgen, BMS, GSK, Janssen, Pfizer, Regeneron, Sanofi, and Stemline; and has participated in an advisory role for AbbVie, Amgen, BMS, GSK, Janssen, Kite, Oncopeptides, Pfizer, Regeneron, Roche, Sanofi, Stemline, and Takeda.

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Long-Term CARTITUDE-4 Update (34 Months): Introduction

- Earlier use of lenalidomide therapy in MM has led to an increase in patients who are lenalidomide refractory after first relapse[1,2]
- Outcomes are poor for patients who are lenalidomide refractory after 1–3 prior LOT, with median OS of 21.5 months[3]
- Cilta-cel is approved in the US and EU for lenalidomide-refractory patients with ≥1 prior LOT based on the CARTITUDE-4 study[4-6]
- In CARTITUDE-4, a single cilta-cel infusion vs SOC significantly improved PFS (weighted HR, 0.26; *P*<0.0001) and ≥CR rate (73.1% vs 21.8%)[4]

We report updated efficacy and safety, including prespecified OS analysis, at a median follow-up of 33.6 months[a]

[a]Data cut-off date: May 1, 2024. Cilta-cel, ciltacabtagene autoleucel; CR, complete response; HR, hazard ratio; LOT, line of therapy; MM, multiple myeloma; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma; SOC, standard of care. 1. de Arriba de la Fuente F, et al. *Cancers (Basel)* 2022;15:155. 2. Moreau P, et al. *Blood Cancer J* 2019;9:38. 3. Hajek R, et al. *Blood* 2022;140 (Suppl 1):7200-2. 4. San-Miguel J, et al. *N Engl J Med* 2023;389:335-47. 5. CARVYKTI® (ciltacabtagene autoleucel). Prescribing information. Horsham, PA: Janssen Biotech, Inc.; 2024. 6. CARVYKTI® (ciltacabtagene autoleucel). European Medicines Agency. Product information. Beerse, Belgium: Janssen-Cilag International NV; 2024

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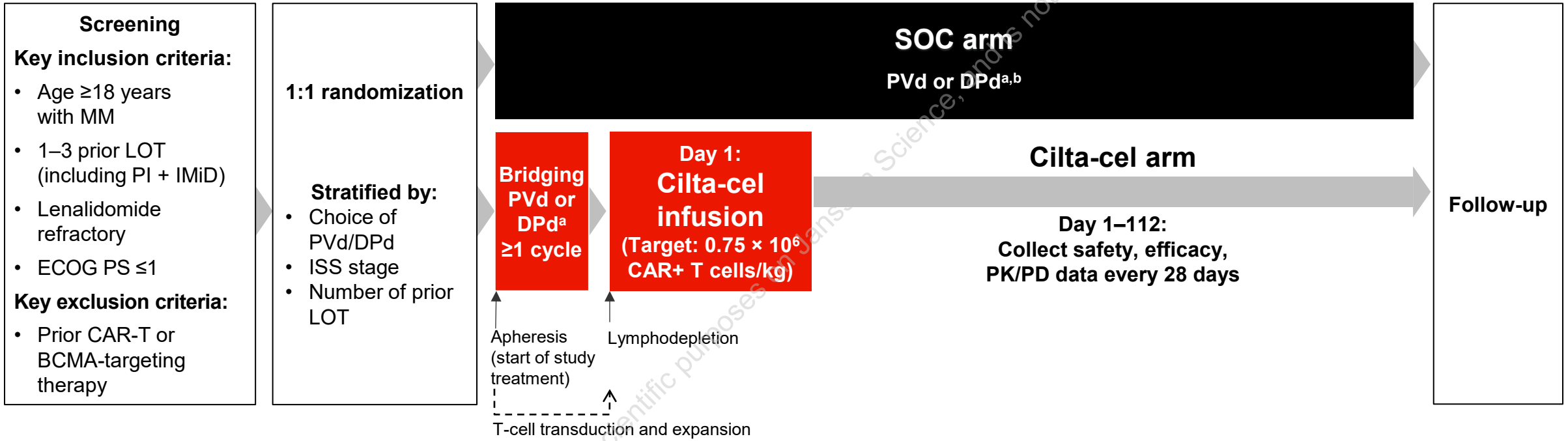
CARTITUDE-4: Study Design and Endpoints[1]



Primary endpoint

- PFS[c,d]

Secondary endpoints

- Efficacy: ≥CR, ORR, MRD negativity, OS[d]
- PROs
- Incidence and severity of AEs[e]

[a]Physicians' choice. [b]Administered until disease progression. [c]Time from randomization to disease progression/death. [d]Prespecified first and second interim analyses performed after approximately 75% or 100% of planned 250 PFS events were accumulated, respectively. [e]Assessed per CTCAE version 5.0. CRS and ICANS were graded per ASTCT criteria. AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; CR, complete response; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; ICANS, immune effector cell–associated neurotoxicity syndrome; IMiD, immunomodulatory drug; ISS, International Staging System; 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. 1. San-Miguel J, et al. *N Engl J Med* 2023;389:335-47.

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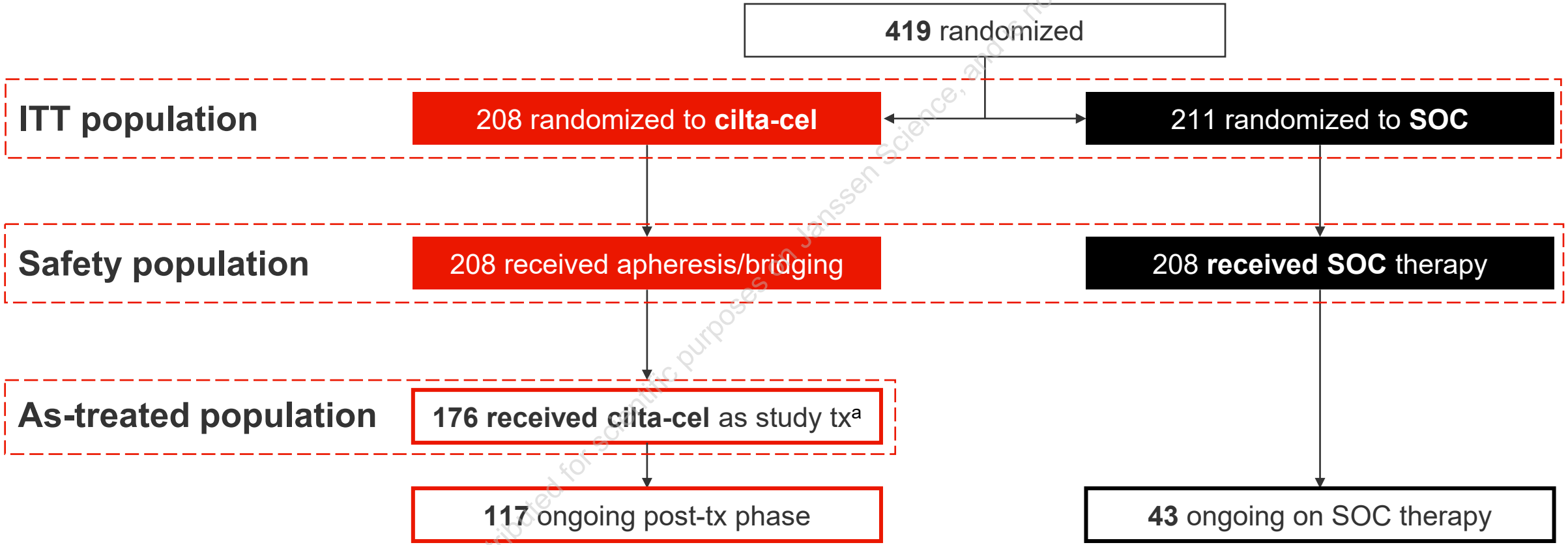
Long-Term CARTITUDE-4 Update (34 Months): Patient Population



- At the May 1, 2024, data cut-off, median follow-up was 33.6 months (range, 0.1–45.0)

[a]32 did not receive cilta-cel as study treatment (n=30 due to disease progression; n=2 due to death during bridging therapy/lymphodepletion), of which 20 received cilta-cel as subsequent LOT.
Cilta-cel, ciltacabtagene autoleucel; ITT, intent-to-treat; LOT, line of therapy; SOC, standard of care; tx, treatment.

CARTITUDE-4:
Baseline Characteristics Generally Balanced Across Arms

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)
ISS stage, n (%)		
I	136 (65.4)	132 (62.6)
II	60 (28.8)	65 (30.8)
III	12 (5.8)	14 (6.6)
Presence of soft tissue plasmacytomas,[a] n (%)	44 (21.2)	35 (16.6)
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,[b] n (%)	123 (59.4)	132 (62.9)
del(17p)	49 (23.7)	43 (20.5)
t(14;16)	3 (1.4)	7 (3.3)
gain/amp(1q)	89 (43.0)	107 (51.0)
2 or more high-risk cytogenetic features	43 (20.8)	49 (23.3)
del(17p), t(14;16), or t(4;14)	73 (35.3)	69 (32.9)
Triple-class exposed,[c] n (%)	53 (25.5)	55 (26.1)
Penta-drug exposed,[d] n (%)	14 (6.7)	10 (4.7)
Refractory status, n (%)		
Triple-class refractory[c,e]	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]Including extramedullary and bone-based plasmacytomas with measurable soft tissue component. [b]In 207 (cilta-cel arm) and 210 (SOC arm) patients. [c]Including 1 PI, 1 IMiD, and 1 anti-CD38 monoclonal antibody. [d]Including ≥2 PIs, ≥2 IMiDs, and 1 anti-CD38 monoclonal antibody. [e]2 patients (cilta-cel arm) and 1 patient (SOC arm) were penta-drug refractory.
Cilta-cel, ciltacabtagene autoleucel; IMiD, immunomodulatory drug; ISS, International Staging System; ITT, intent-to-treat; LOT, line of therapy; PI, proteasome inhibitor; SOC, standard of care.

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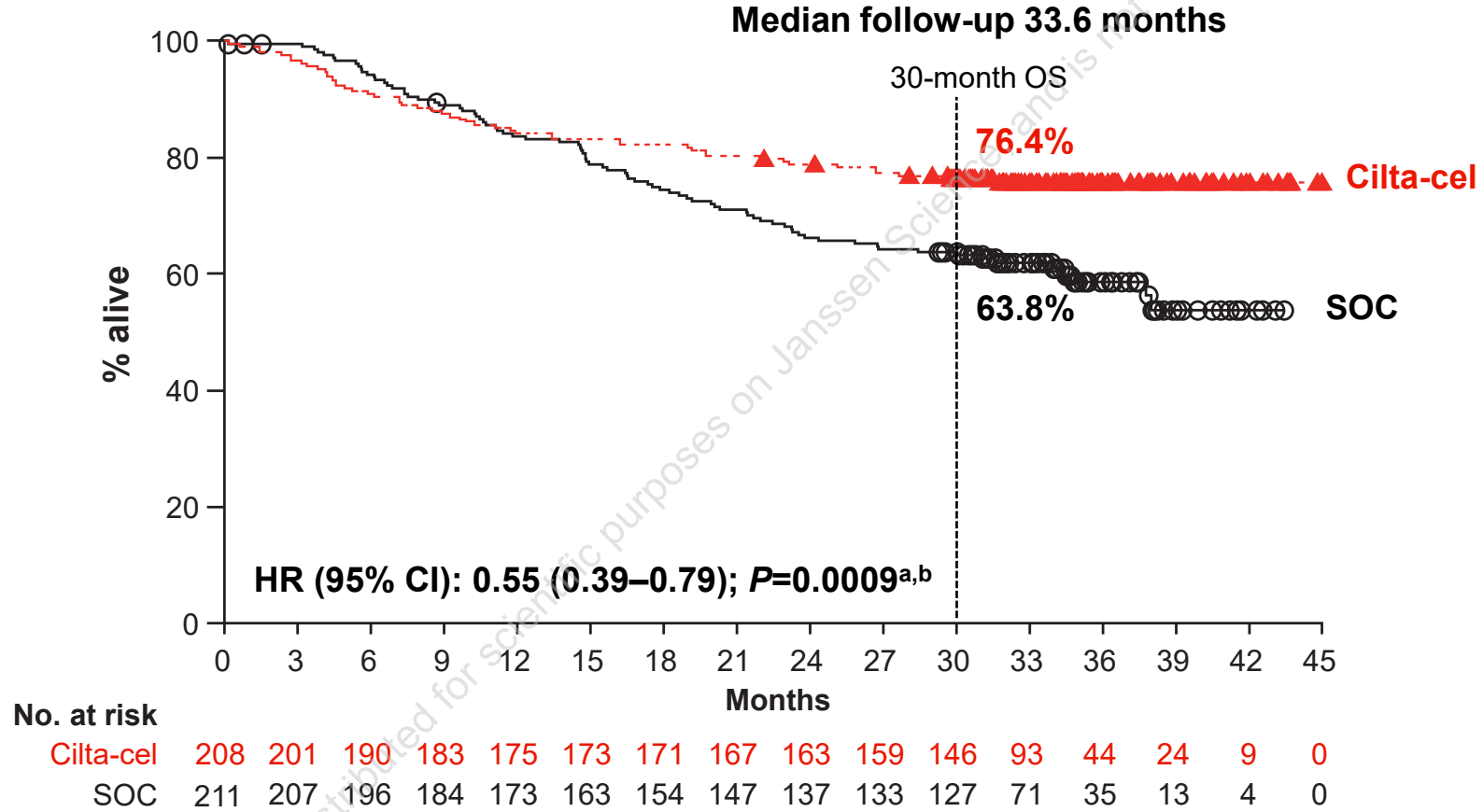
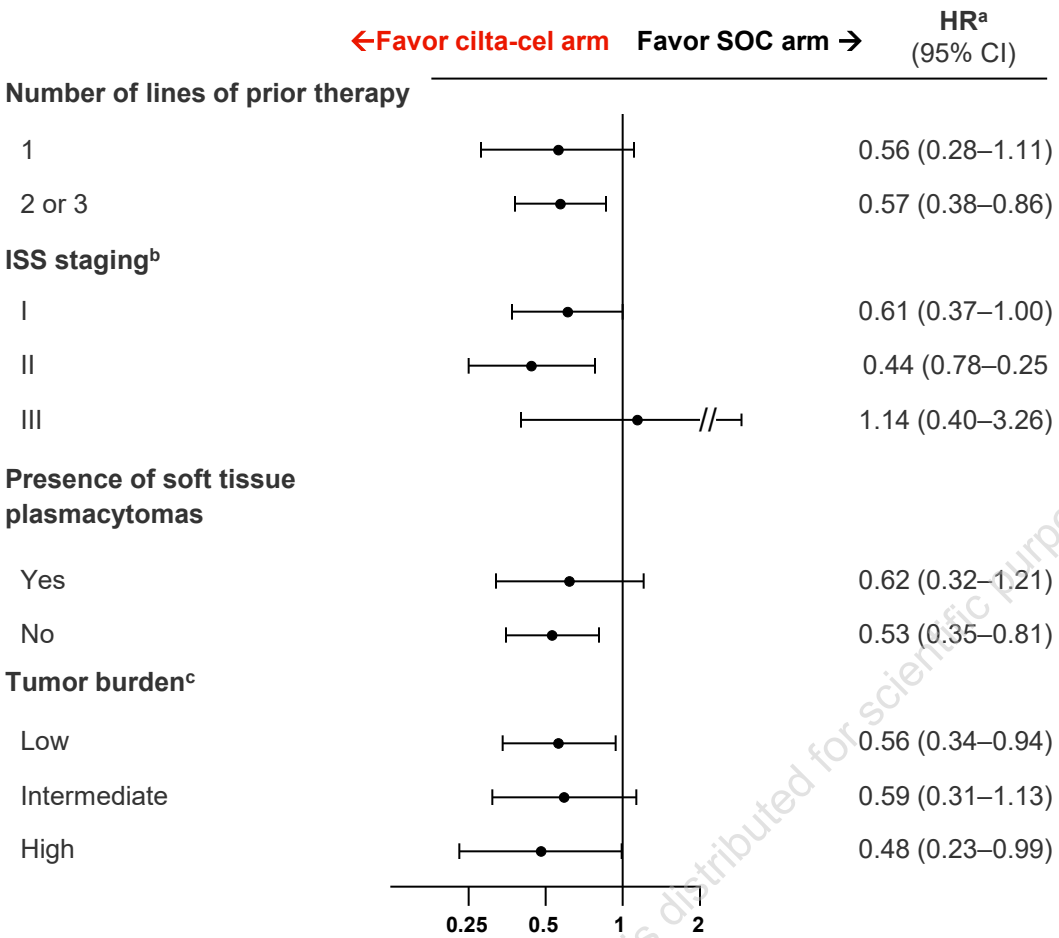
Long-Term CARTITUDE-4 Update (34 Months): Cilta-cel Significantly Improved Overall Survival

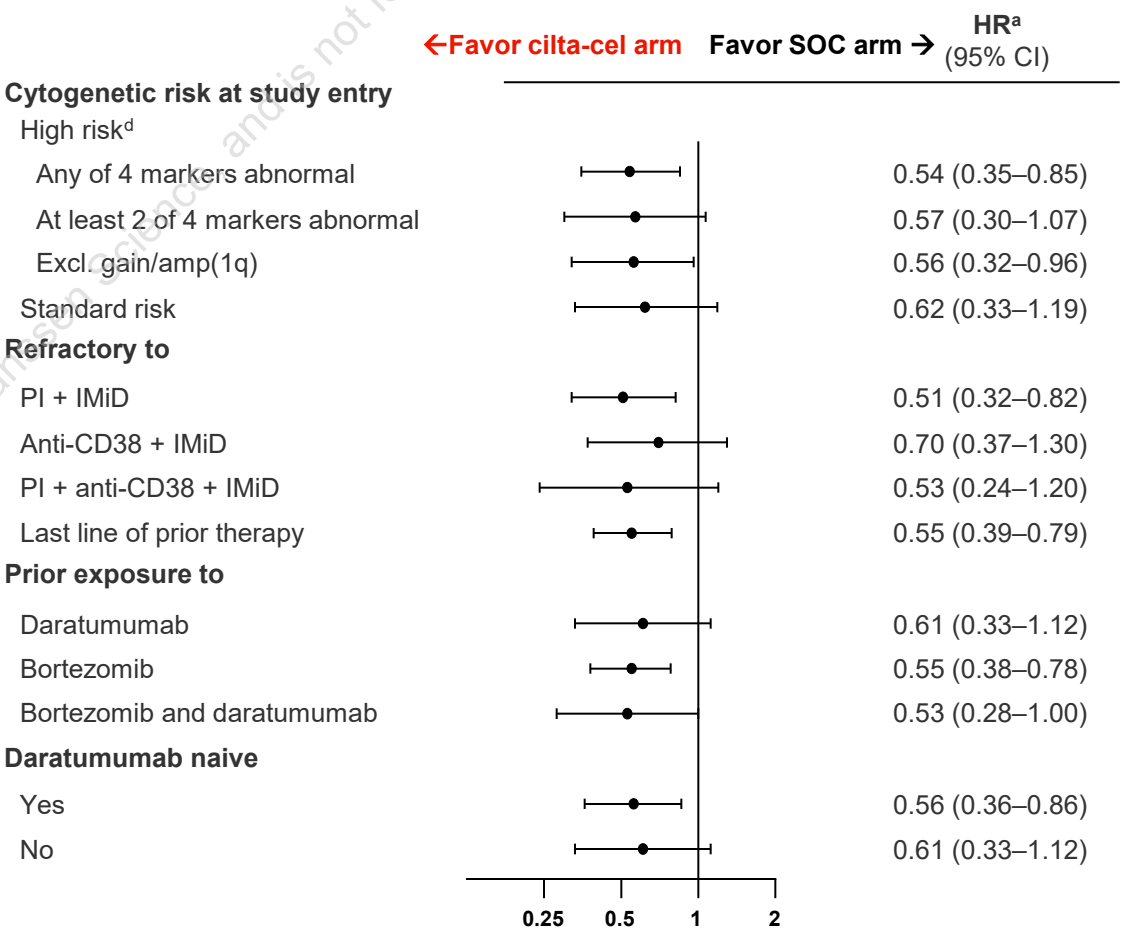


First CAR-T to demonstrate overall survival benefit in multiple myeloma

[a]Log-rank test. *P*-value, 0.0009, crossed the prespecified boundary of 0.0108 as implemented by the Kim-DeMets spending function with parameter=2. [b]Hazard ratio and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable.
CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; OS, overall survival; SOC, standard of care.

Long-Term CARTITUDE-4 Update (34 Months): Consistent Overall Survival Benefit for Cilta-cel Across Prespecified Subgroups





Consistent reduction in risk of death across prespecified subgroups[e]

[a]HR and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable. HR <1 indicates an advantage for the cilta-cel arm. [b]Based on serum β_2-microglobulin and albumin. [c]Low tumor burden defined as meeting all following parameters (as applicable): bone marrow % plasma cell <50%, serum M-protein <3 g/dL, serum free light chain <3000 mg/L; high tumor burden defined as meeting any of the following parameters: bone marrow % plasma cell ≥80%, serum M-protein ≥5 g/dL, serum free light chain ≥5000 mg/L; intermediate tumor burden did not fit either criteria of high or low tumor burden. [d]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". [e]Except ISS stage III, which had n=12 in cilta-cel arm and n=14 in SOC arm.
Cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; IMiD, immunomodulatory drug; ISS, International Staging System; OS, overall survival; PI, proteasome inhibitor; SOC, standard of care.

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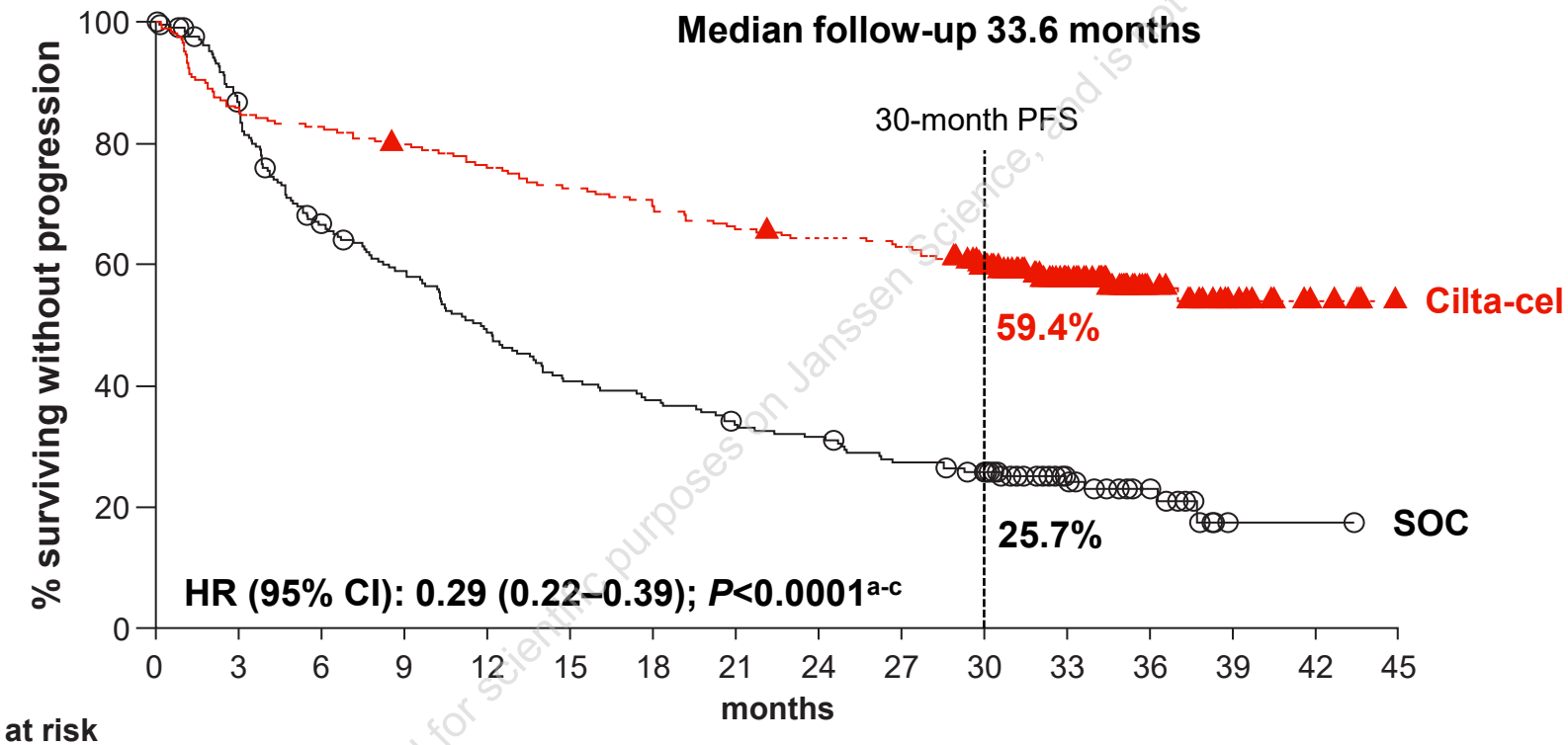
Long-Term CARTITUDE-4 Update (34 Months): Cilta-cel Maintained Significant Improvement in Progression-Free Survival



No. at risk																
Cilta-cel	208	177	172	165	157	150	145	136	132	129	111	65	29	13	5	0
SOC	211	176	133	116	96	80	74	65	61	52	47	25	12	1	1	0

~70% reduction in the risk of progression or death in patients who received cilta-cel and mPFS has not been reached

[a]Constant piecewise weighted log-rank test. [b]HR and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable, including only PFS events that occurred >8 weeks post randomization.
[c]Nominal *P* value.
Cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; mPFS, median progression-free survival; PFS, progression-free survival; SOC, standard of care.

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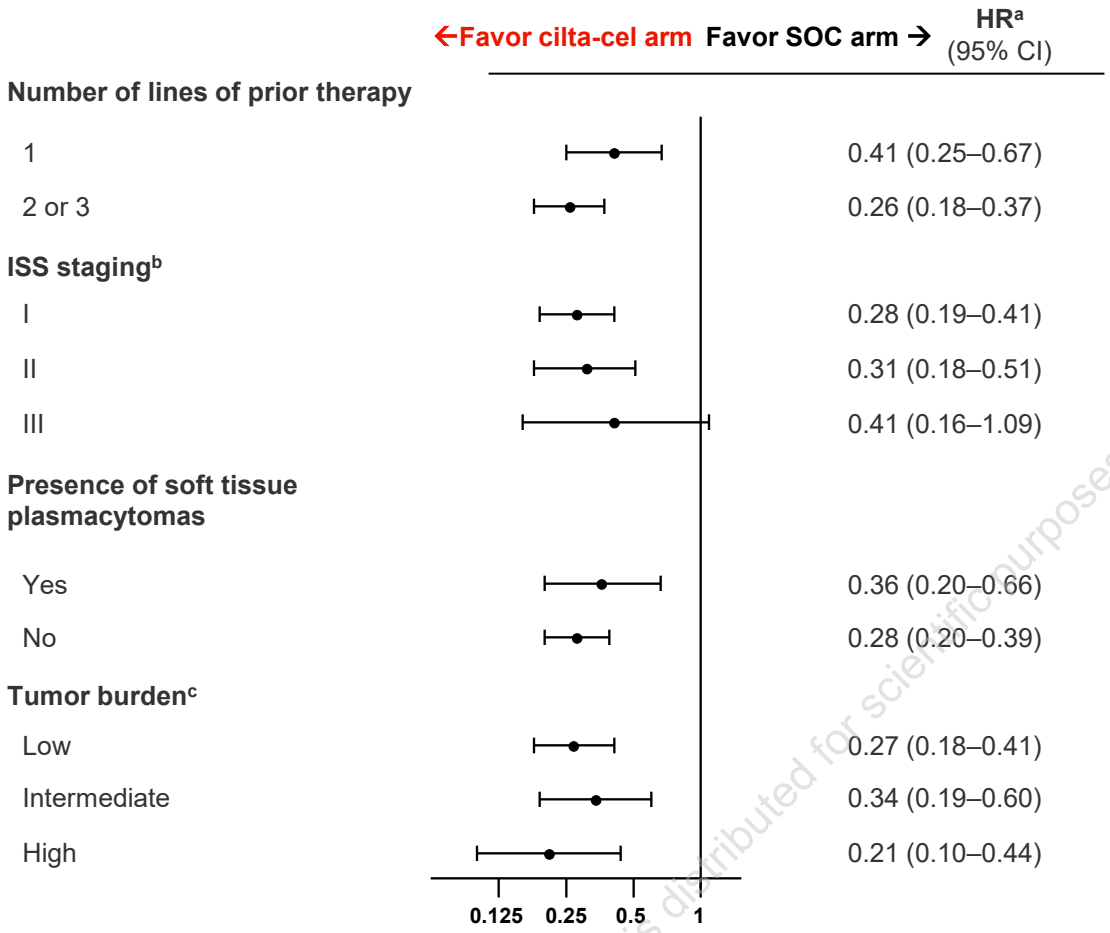
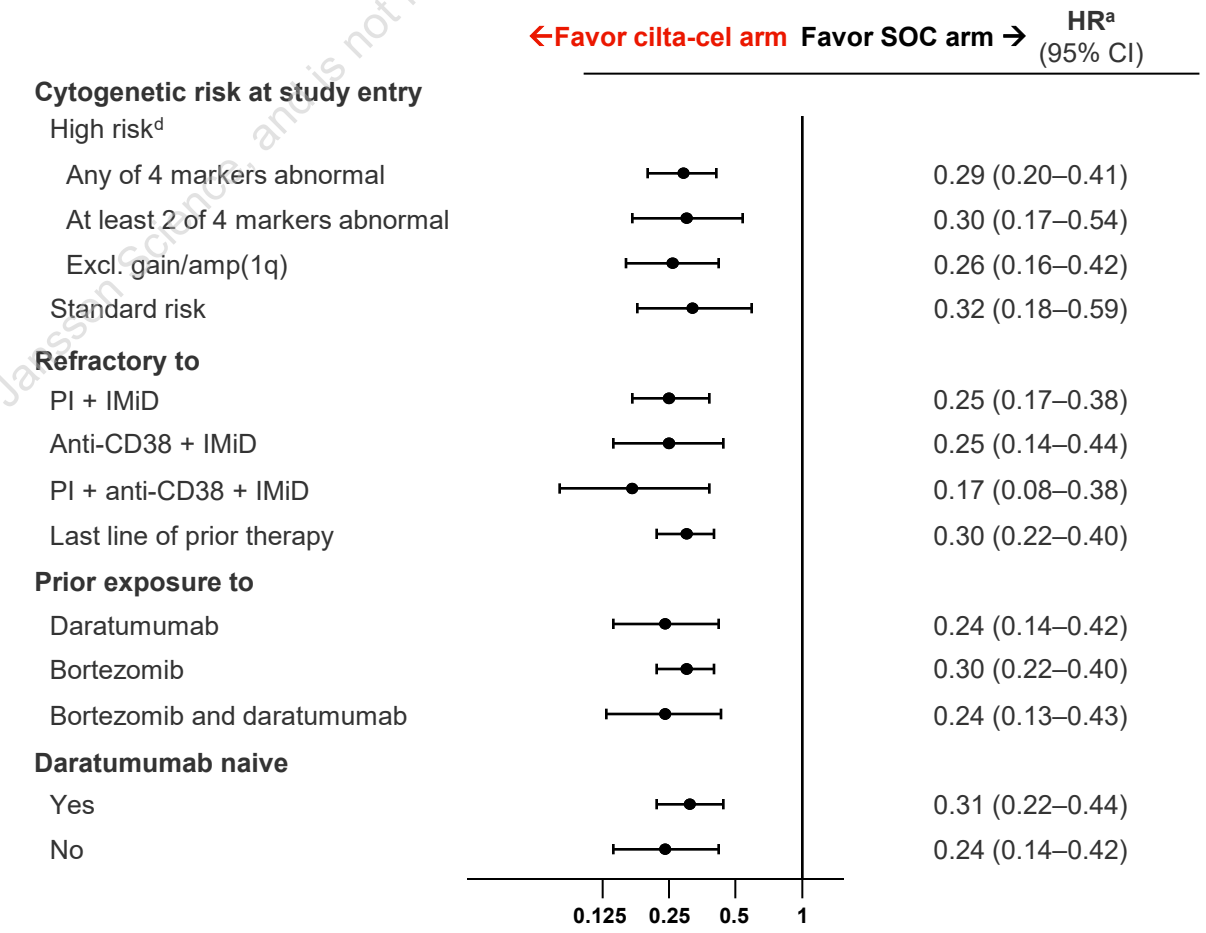
Long-Term CARTITUDE-4 Update (34 Months): Consistent Progression-Free Survival Benefit for Cilta-cel Across All Prespecified Subgroups





Consistent reduction in the risk of progression or death across all prespecified subgroups

[a]HR and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable, including only PFS events that occurred >8 weeks post randomization. [b]Based on serum β_2-microglobulin and albumin. [c]Low tumor burden defined as meeting all following parameters (as applicable): bone marrow % plasma cell <50%, serum M-protein <3 g/dL, serum free light chain <3000 mg/L; high tumor burden defined as meeting any of the following parameters: bone marrow % plasma cell ≥80%, serum M-protein ≥5 g/dL, serum free light chain ≥5000 mg/L; intermediate tumor burden did not fit either criteria of high or low tumor burden. [d]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; HR, hazard ratio; IMiD, immunomodulatory drug; ISS, International Staging System; PFS, progression-free survival; PI, proteasome inhibitor; SOC, standard of care;

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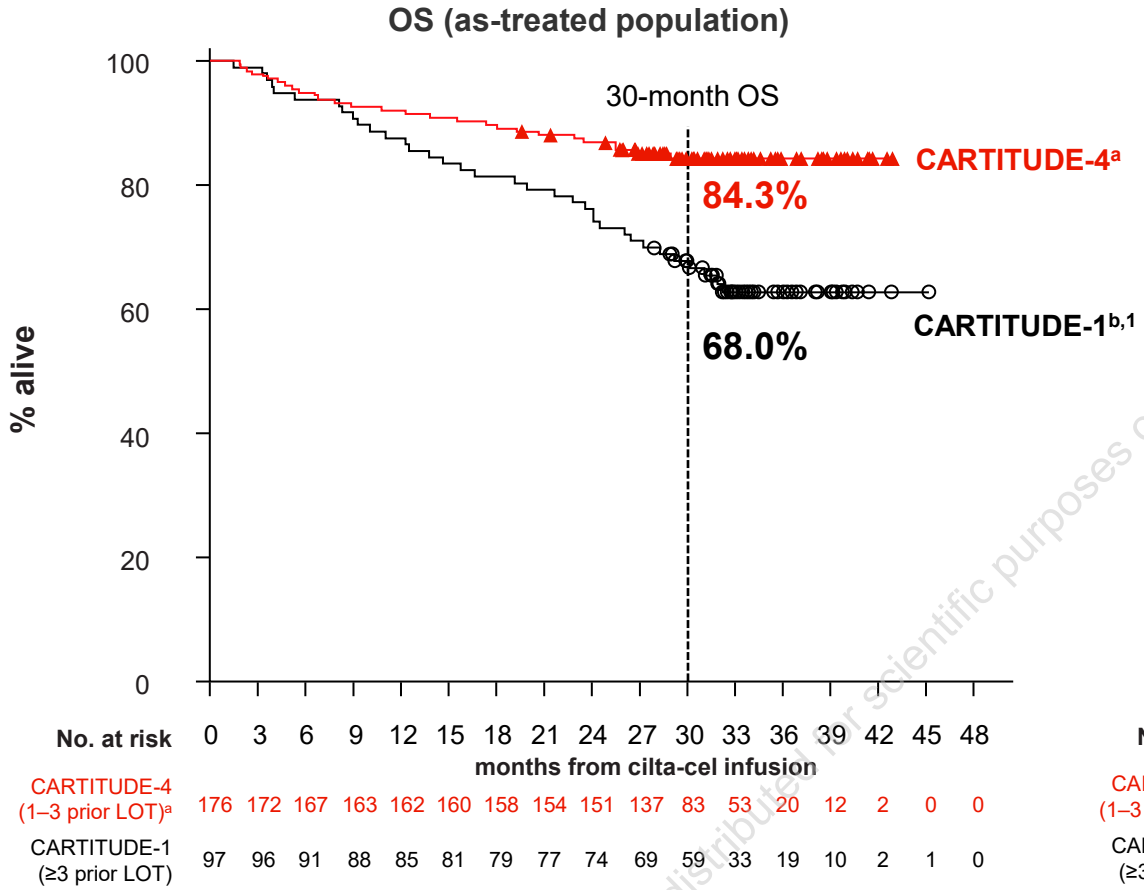
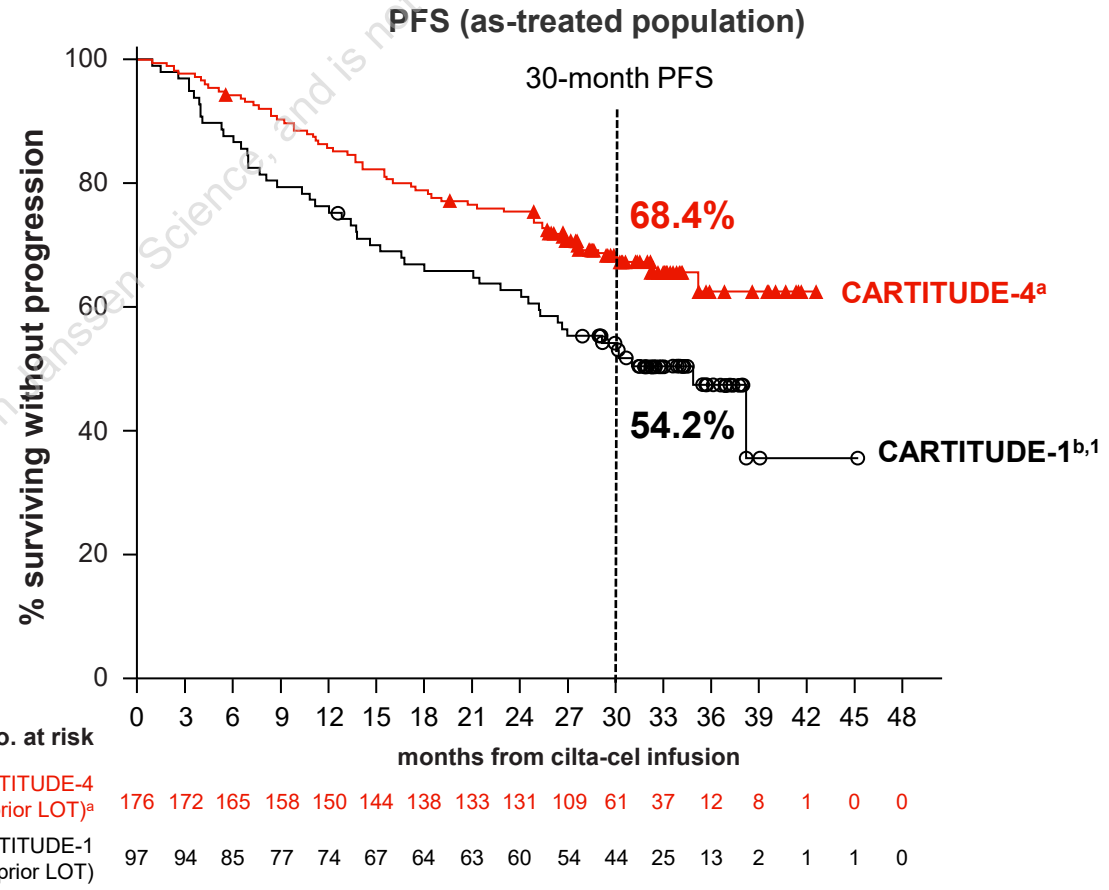
Long-Term CARTITUDE-4 Update (34 Months): Numerically Higher Overall and Progression-Free Survival Rates Versus CARTITUDE-1



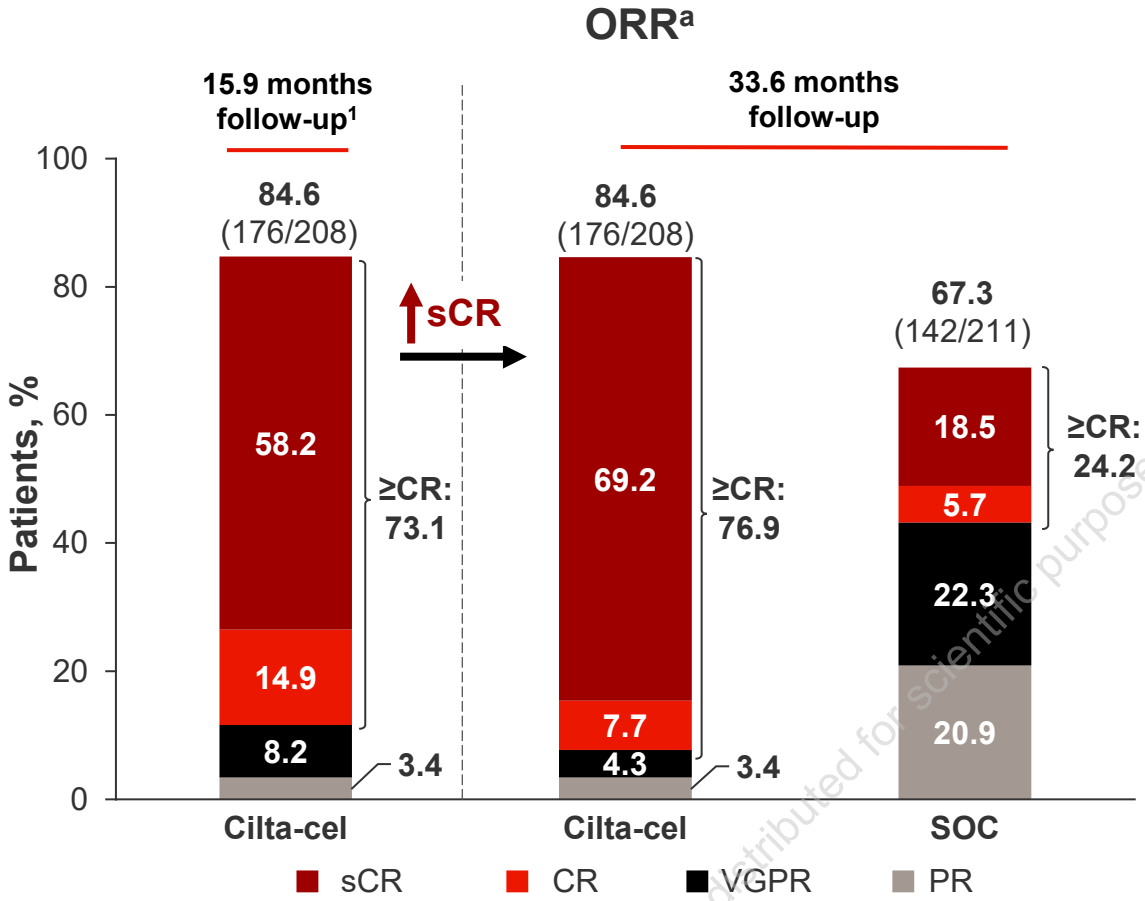


Cilta-cel use in earlier lines demonstrated numerically higher rates of overall and progression-free survival

[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 30.5 months. [b]33.4-month median follow-up.
Cilta-cel, ciltacabtagene autoleucel; LOT, line of therapy; OS, overall survival; PFS, progression-free survival; SOC, standard of care.

1. Lin et al. Abstract 8009, presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual.

Long-Term CARTITUDE-4 Update (34 Months): Increased Rates of Deep Responses Seen With Additional Follow-Up With Cilta-cel



DOR[b]

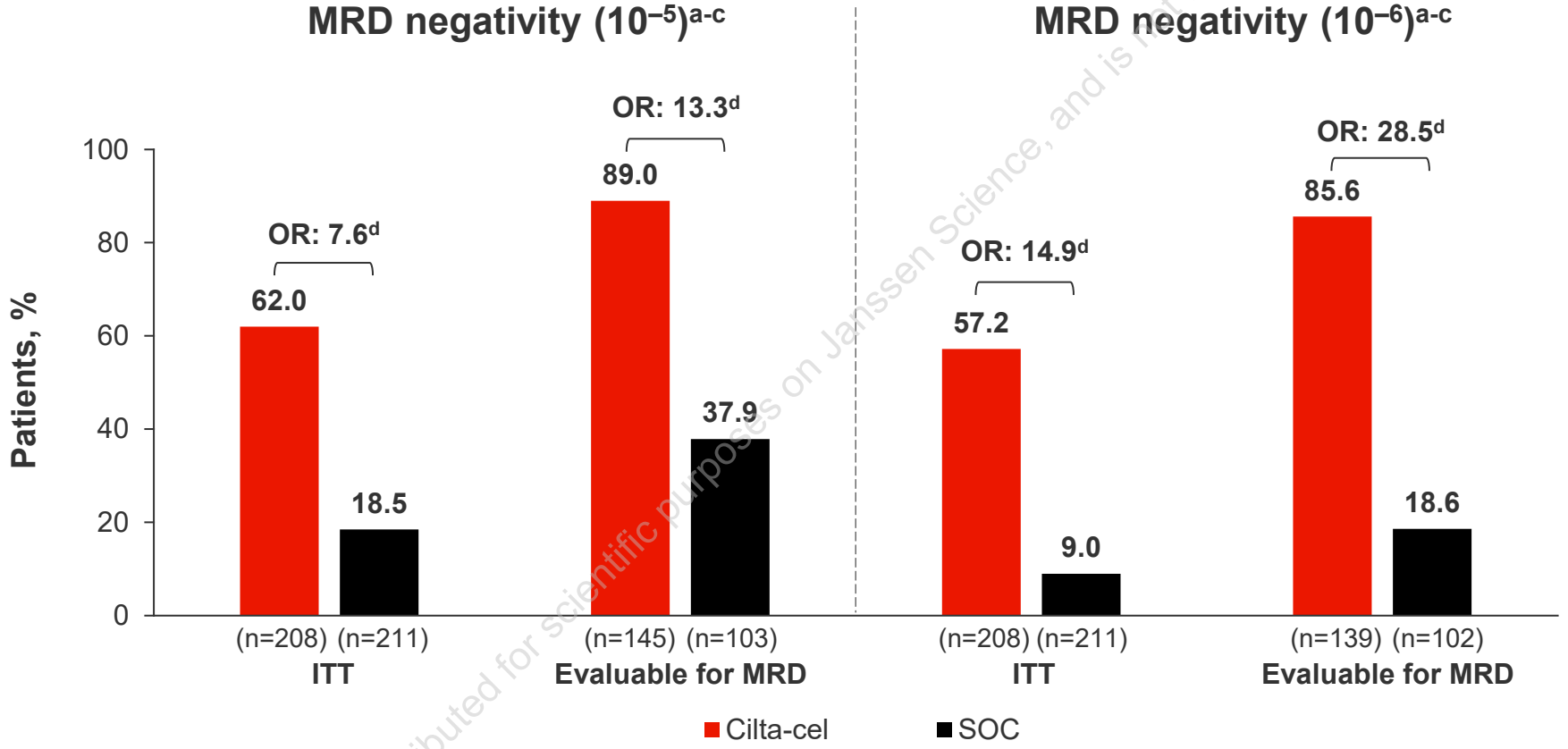
	Cilta-cel	SOC
DOR, months, median (95% CI)	**NR (NE–NE)**	**18.7 (12.9–23.7)**
30-month DOR rate, % (95% CI)	67.4 (59.7–74.0)	35.5 (27.6–43.6)

Cilta-cel provided high ORR and sCR/CR rate with sustained DOR

[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]Analyzed among responders. 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.

1. San-Miguel J, et al. *N Engl J Med* 2023;389:335-47.

Long-Term CARTITUDE-4 Update (34 Months): Cilta-cel Provided Significantly Higher Rate of MRD Negativity



Cilta-cel increased MRD negativity more than 2-fold at 10^{-5}, and more than 4-fold at 10^{-6} vs SOC

[a]Assessed by next-generation sequencing. [b]Proportion of patients who have MRD-negative status (at 10^{-5} or 10^{-6}) by bone marrow aspirate at any time after the date of randomization and prior to progressive disease or subsequent antimyeloma therapy. [c]Evaluable samples were those that passed calibration and quality control and included sufficient cells for evaluation at the respective testing threshold. [d]Stratified Cochran Mantel-Haenszel test. Cilta-cel, ciltacabtagene autoleucel; ITT, intent-to-treat; MRD, minimal residual disease; OR, odds ratio; SOC, standard of care.

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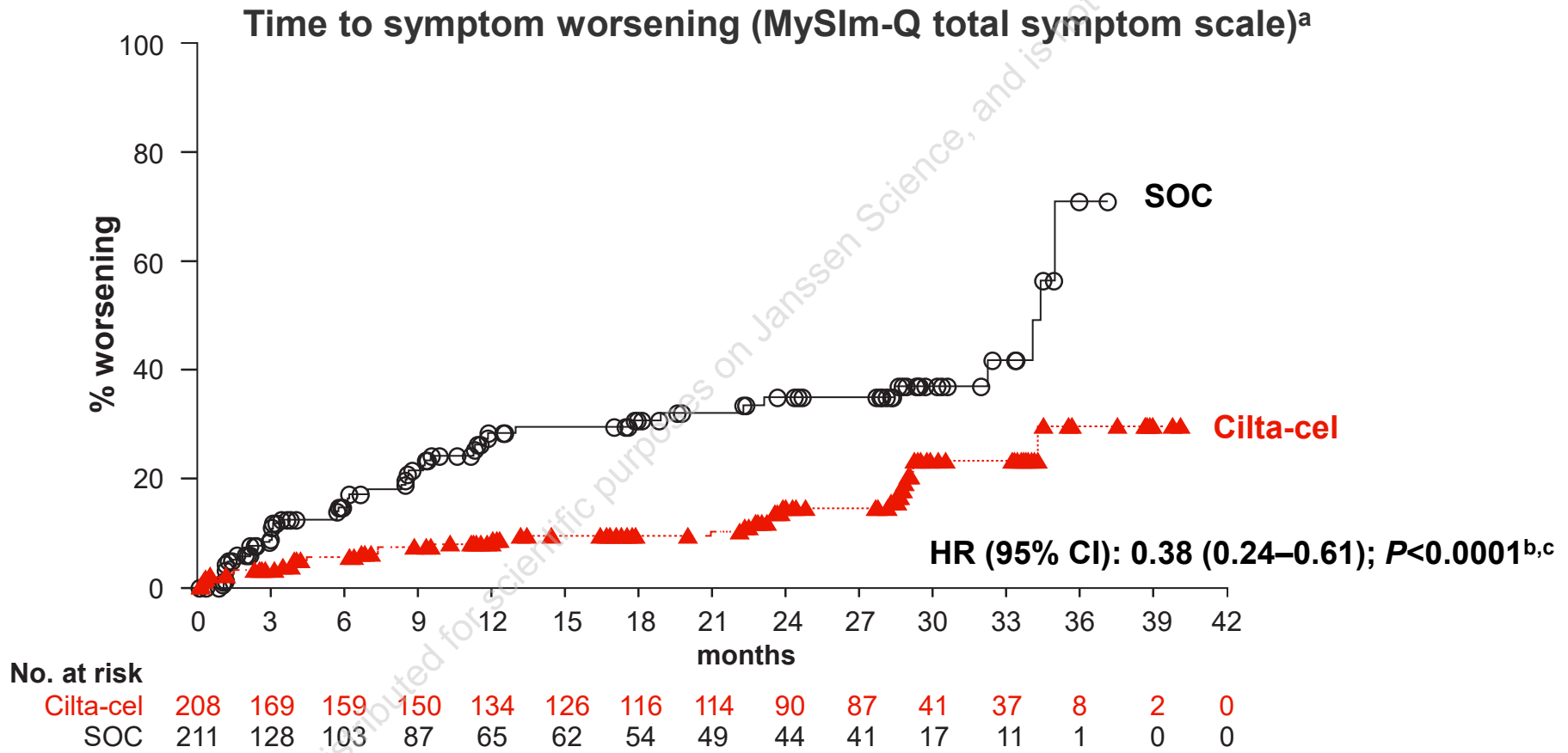
Long-Term CARTITUDE-4 Update (34 Months): Cilta-cel Significantly Extended Time to Symptom Worsening



Cilta-cel improved QoL vs SOC by extending time to symptom worsening

[a]Median follow-up, 33.6 months. [b]Log-rank test. [c]HR and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable.
Cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; QoL, quality of life; SOC, standard of care.

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Long-Term CARTITUDE-4 Update (34 Months): Safety Profile Consistent With Previous Analysis

Infections	Cilta-cel (n=208)	SOC (n=208)
Treatment-emergent infections, %		
All grade	63.5	76.4
Grade 3/4	28.4	29.8
Deaths due to TE- and non-TE infections, n	16	19
In first year, n	13	8
In second year, n	2	8

Cause of death	Cilta-cel (n=208)	SOC (n=208)
Deaths, n	**50**	**82**
Due to progressive disease	21	51
Due to TEAE	12	8

- **Both arms had grade 3/4 TEAE around 97%; most frequently cytopenia**

SPM	Cilta-cel (n=208)	SOC (n=208)
SPMs, n (%)	**27 (13.0)**	**24 (11.5)**
Hematologic[a]	7 (3.4)	1 (0.5)
MDS, n	4	0
Progressed to AML, n	2	–
AML, n	1	0
Peripheral T-cell lymphoma, n	2	0
EBV-associated lymphoma, n	0	1
Cutaneous/non-invasive[a]	15 (7.2)	15 (7.2)
Non-cutaneous/invasive[a]	6 (2.9)	8 (3.8)

- **No new cases of cranial nerve palsy or MNT for the cilta-cel arm since the previous report[1]**

[a]Multiple SPMs could occur in the same patient.
AML, acute myeloid lymphoma; cilta-cel, ciltacabtagene autoleucel; CNP, cranial nerve palsy; EBV, Epstein-Barr virus; MDS, myelodysplastic syndrome; MNT, movement and neurocognitive treatment-emergent adverse event; TE, treatment-emergent; TEAE, treatment-emergent adverse event; SOC, standard of care; SPM, second primary malignancy.

1. San-Miguel J, et al. *N Engl J Med* 2023;389:335-47.

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Long-Term CARTITUDE-4 Update (34 Months): Conclusions

- Cilta-cel is the first CAR-T cell therapy to show significant OS benefit in MM
  - 45% reduction in the risk of death with cilta-cel vs SOC in patients with lenalidomide-refractory MM after 1–3 prior LOT
  - Consistent OS benefit across subgroups
- Median OS and PFS were not reached with cilta-cel
- QoL was significantly improved with cilta-cel vs SOC
- Safety profile was consistent with previous analysis

A one-time cilta-cel infusion significantly prolonged OS and improved QoL

CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; LOT, line of therapy; MM, multiple myeloma; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; OS, overall survival; PFS, progression-free survival; QoL, quality of life; SOC, standard of care.

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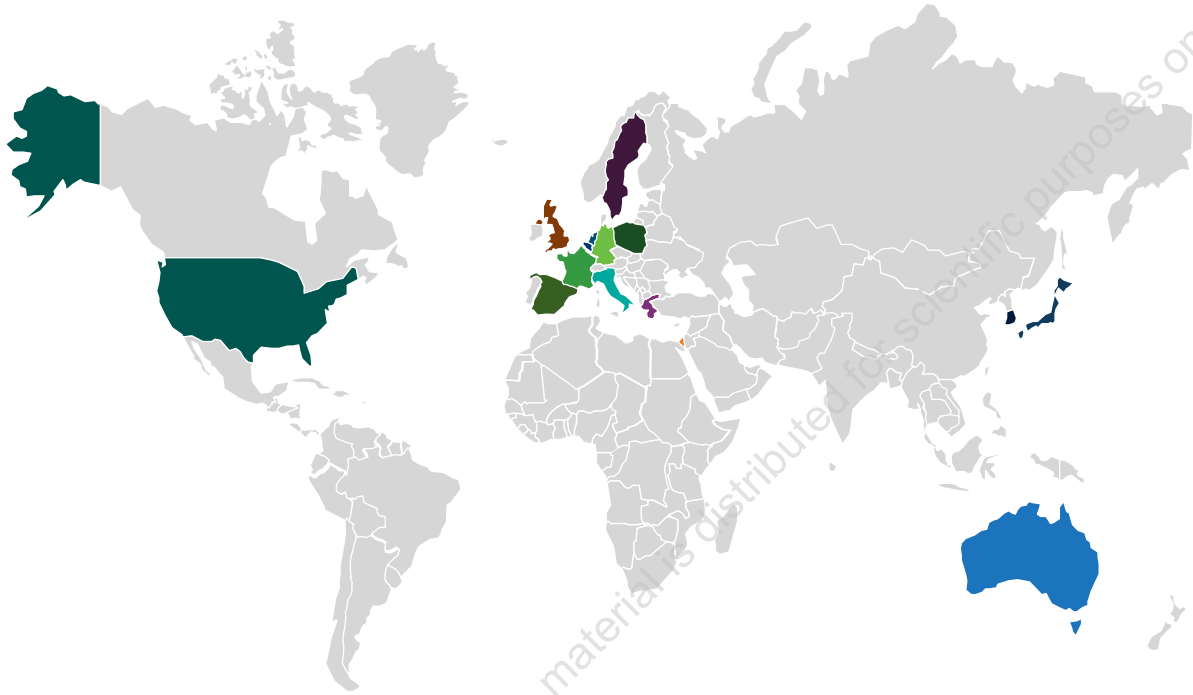
- Medical writing support was provided by Joy Lin, PhD, of Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC



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Dominik Dytfeld
Ewa Lech-maranda
Sebastian Giebel
Magdalena Dutka

Republic of Korea
Seok Jin Kim
Chang-Ki Min
Sung-soo Yoon

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Sweden
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USA
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Surbhi Sidana
Iris Isufi
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Binod Dhakal
Yi Lin
Natalie Callander
Urvi Shah
Saurabh Chhabra

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