Long-Term Progression-Free Survival Benefit With Ciltacabtagene Autoleucel in Standard-Risk Relapsed/Refractory Multiple Myeloma

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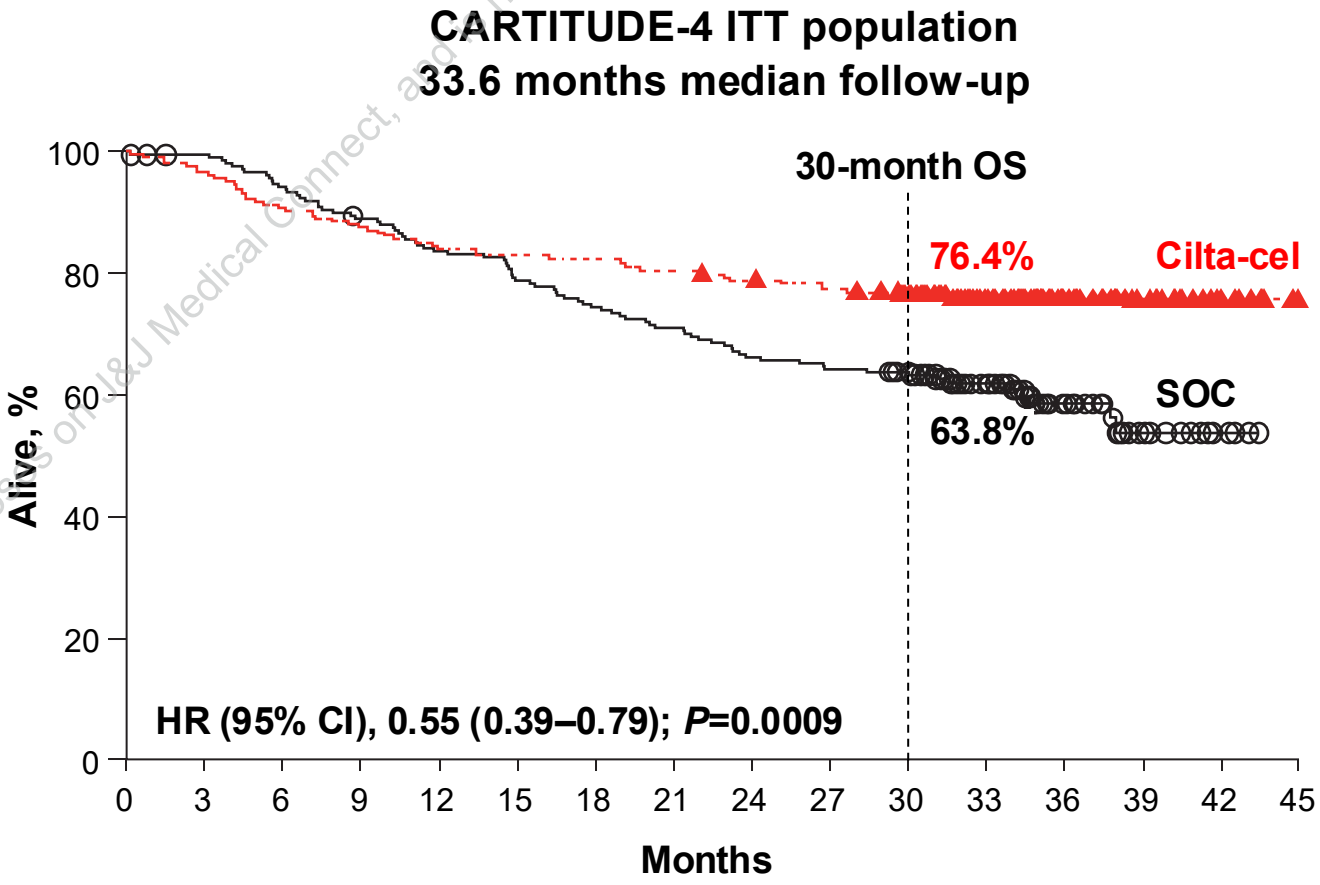
Introduction

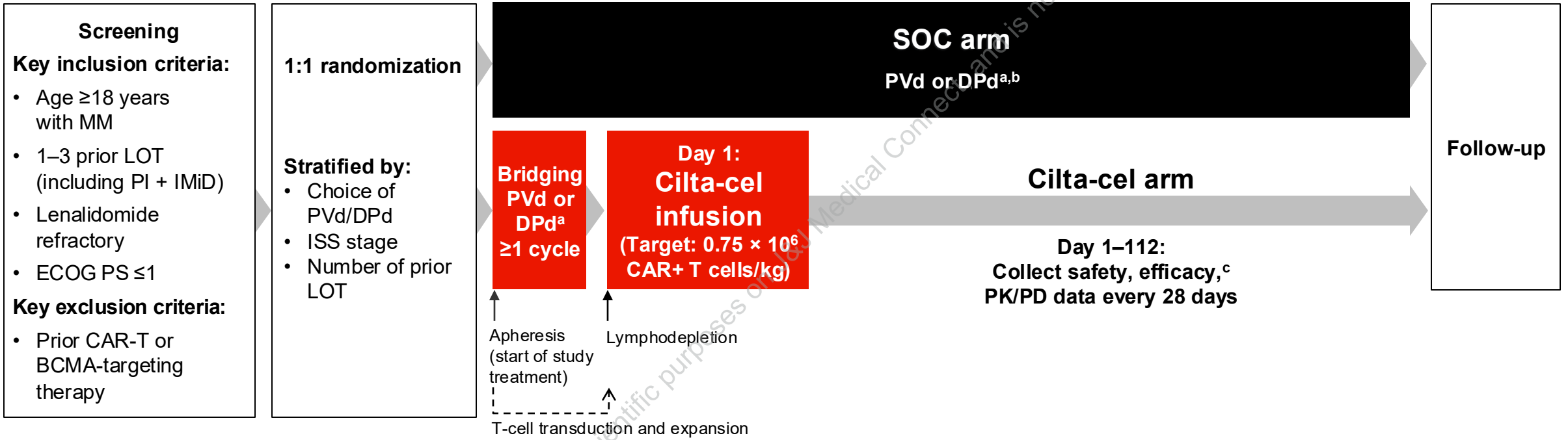
- In CARTITUDE-1, one-third of patients with MM (≥3 prior LOT) were treatment- and progression- free for ≥5 years after a single infusion, providing the first evidence that cilta-cel is potentially curative in RRMM[1]
- Cilta-cel significantly improved PFS and OS vs SOC in earlier-line RRMM population in CARTITUDE-4[2,3]
  - PFS and OS benefits vs SOC were consistent in patients with high-risk cytogenetics[3] and functionally high-risk patients[4]
- Patients with standard-risk RRMM[5,6] and patients with early sustained MRD response[7] may have the highest likelihood of cure
- Here, we report outcomes in CARTITUDE-4 patients with standard-risk cytogenetics[5]



cilta-cel, ciltacabtagene autoleucel; ITT, intent-to-treat; LOT, line of therapy; MM, multiple myeloma; MRD, minimal residual disease; RRMM, relapsed/refractory multiple myeloma.

1. Jagannath S, et al. *J Clin Oncol* 2025;43:2766-71. 2. San-Miguel J, et al. *N Engl J Med* 2023;389:339-47. 3. Mateos M-V, et al. *Clin Lymphoma Myeloma Leuk* 2024;24(suppl 2):S290. 4. Costa LJ, et al. Presented at ASCO; May 31–June 4, 2024; Chicago, IL, USA & Virtual. 5. Sidana S, et al. *J Clin Oncol* 2025;43:7539. 6. Sidana S, et al. *Blood* 2025;145:85-97. 7. Popat R, et al. *Blood* 2024;144(Suppl 1):1032.

CARTITUDE-4: Study Design[1]



Primary endpoint

- PFS[d]

Secondary endpoints

- Efficacy: ≥CR, ORR, MRD negativity, OS
- Incidence and severity of AEs

[a]Physician's choice. [b]Administered until disease progression. [c]Efficacy data were collected after Day 112 every 28 days. [d]Time from randomization to disease progression/death. AE, adverse event; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CTCAE, Common Terminology Criteria for Adverse Events; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; ISS, International Staging System; ORR, overall response rate; PD, pharmacodynamics; PI, proteasome inhibitor; PK, pharmacokinetics; PVd, pomalidomide, bortezomib, and dexamethasone. 1. San-Miguel J, et al. *N Engl J Med* 2023;389:335-47.

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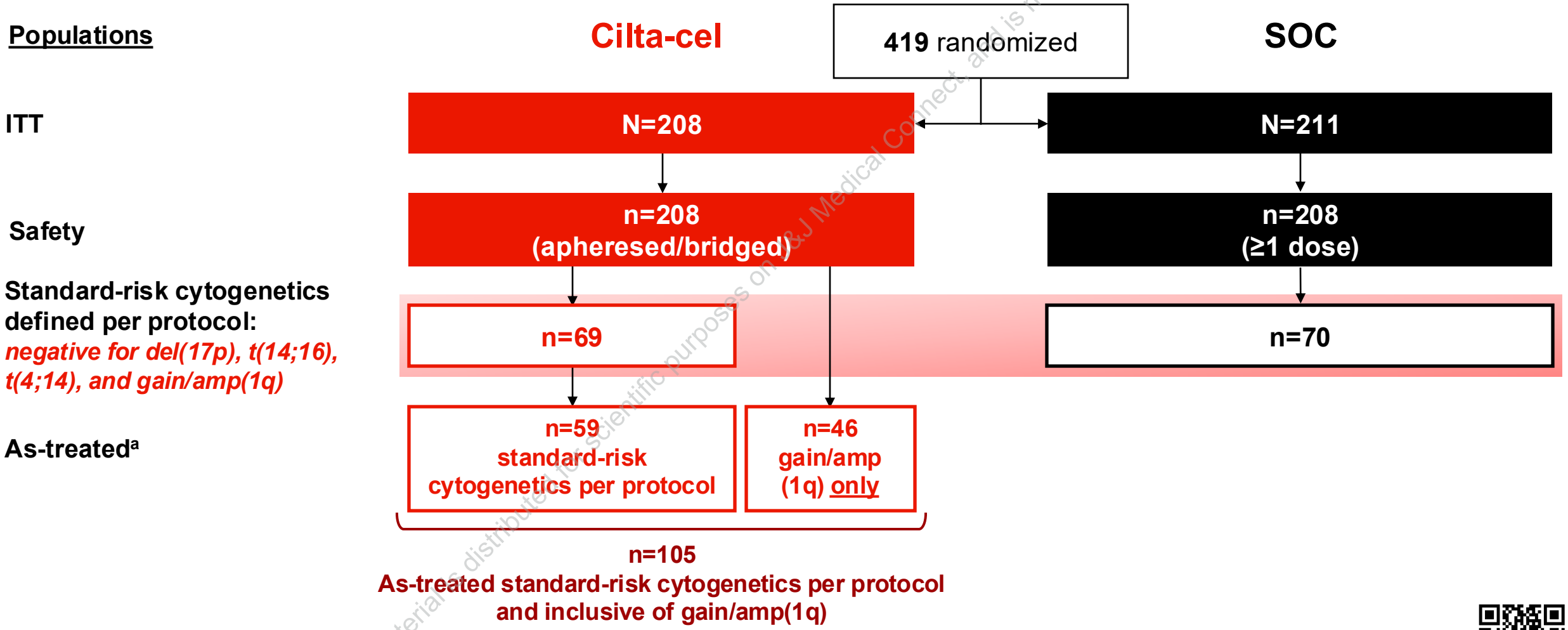
CARTITUDE-4: Study Population



[a]10 patients with standard-risk cytogenetics did not receive cilta-cel as study treatment due to disease progression prior to cilta-cel infusion.

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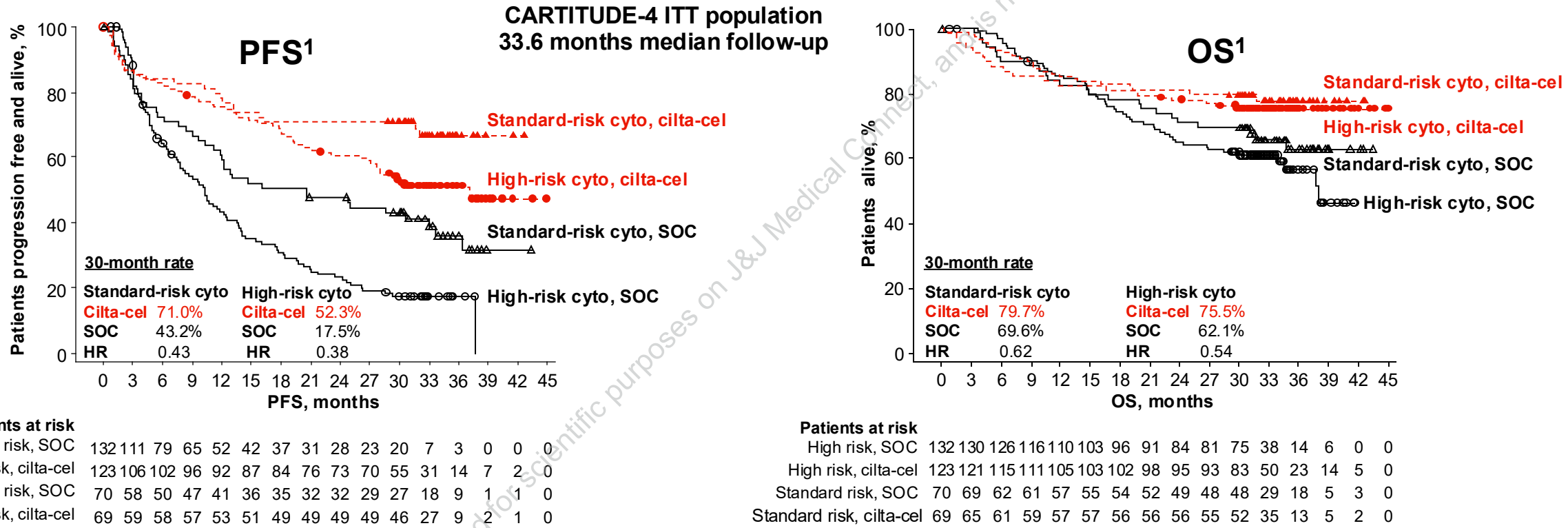
PFS and OS in Patients With High-Risk and Standard-Risk Cytogenetics (ITT)



Patients at risk

High risk, SOC	132	111	79	65	52	42	37	31	28	23	20	7	3	0	0	0
High risk, cilta-cel	123	106	102	96	92	87	84	76	73	70	55	31	14	7	2	0
Standard risk, SOC	70	58	50	47	41	36	35	32	32	29	27	18	9	1	1	0
Standard risk, cilta-cel	69	59	58	57	53	51	49	49	49	49	46	27	9	2	1	0

Patients at risk

High risk, SOC	132	130	126	116	110	103	96	91	84	81	75	38	14	6	0	0
High risk, cilta-cel	123	121	115	111	105	103	102	98	95	93	83	50	23	14	5	0
Standard risk, SOC	70	69	62	61	57	55	54	52	49	48	48	29	18	5	3	0
Standard risk, cilta-cel	69	65	61	59	57	57	56	56	56	55	52	35	13	5	2	0

In CARTITUDE-4, cilta-cel improved PFS and OS in prespecified subgroups with standard- and high-risk cytogenetics[1]

1. Sidana S, et al. *J Clin Oncol* 2025;43:7539.

CARTITUDE-4 and CARTITUDE-1: Baseline Characteristics of Patients With Standard-Risk Cytogenetics

Baseline characteristics	C-4 Standard-risk cytogenetics (As-treated)		C-1 Standard-risk cytogenetics
	Cilta-cel, n=59 [no gain/amp(1q)]	Cilta-cel, n=105 [+ gain/amp(1q)]	Cilta-cel, n=68 [includes gain/amp(1q)]
Age, median (range), years	61.0 (27–78)	62.0 (27–78)	60.5 (43–78)
Male, n (%)	33 (55.9)	55 (52.4)	39 (57.4)
ISS stage, n (%) I	44 (74.6)	75 (71.4)	40 (58.8)
II	12 (20.3)	25 (23.8)	15 (22.1)
III	3 (5.1)	5 (4.8)	13 (19.1)
Soft tissue plasmacytomas, n (%)	3 (5.1)	6 (5.7)	11 (16.2)
Prior LOTs 1, n (%)	20 (33.9)	33 (31.4)	0
2, n (%)	22 (37.3)	42 (40.0)	0
3, n (%)	17 (28.8)	30 (28.6)	11 (16.2)
Median (range)	2.0 (1–3)	2.0 (1–3)	6.0 (3–18)
Refractory status, n (%) Lenalidomide	59 (100.0)	105 (100.0)	53 (77.9)
Daratumumab	9 (15.3)	21 (20.0)	66 (97.1)
Triple class	5 (8.5)	11 (10.5)	61 (89.7)

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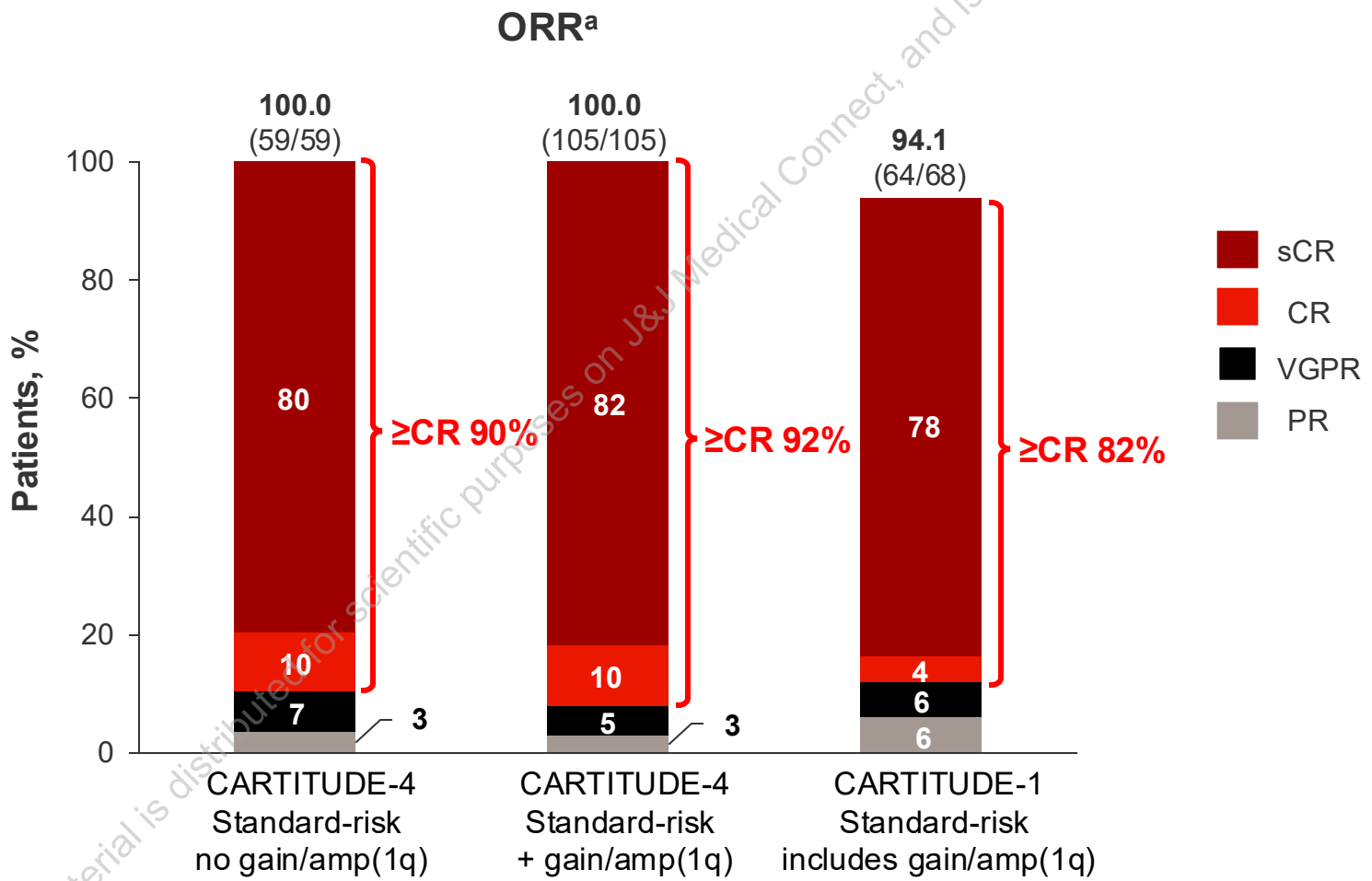
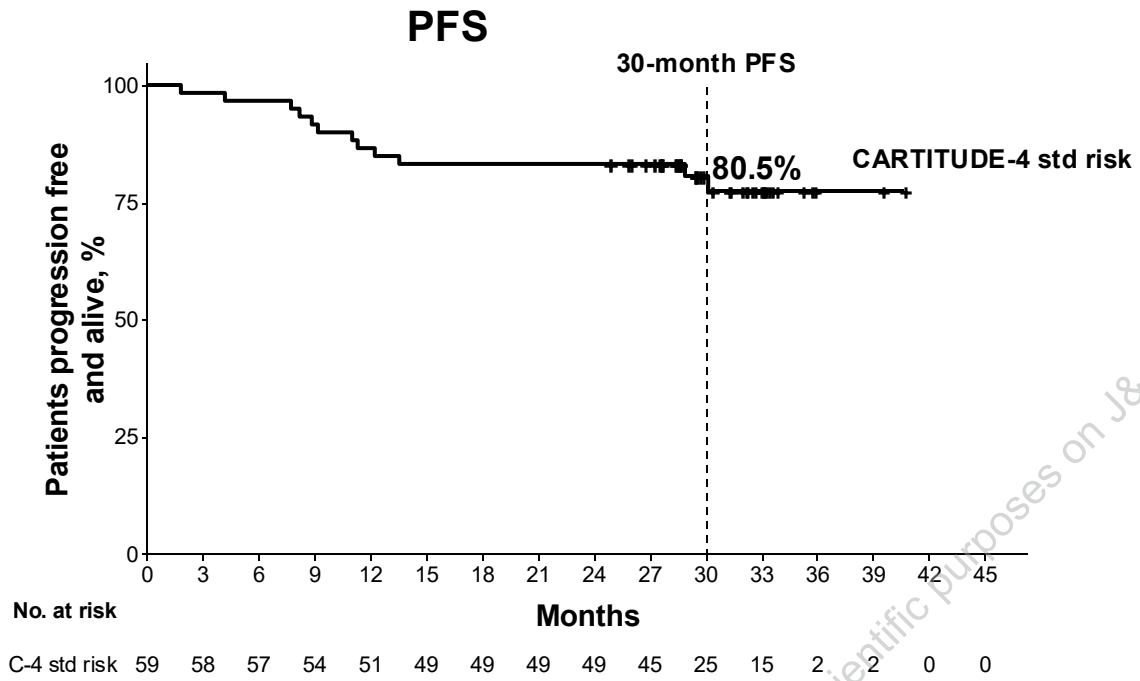
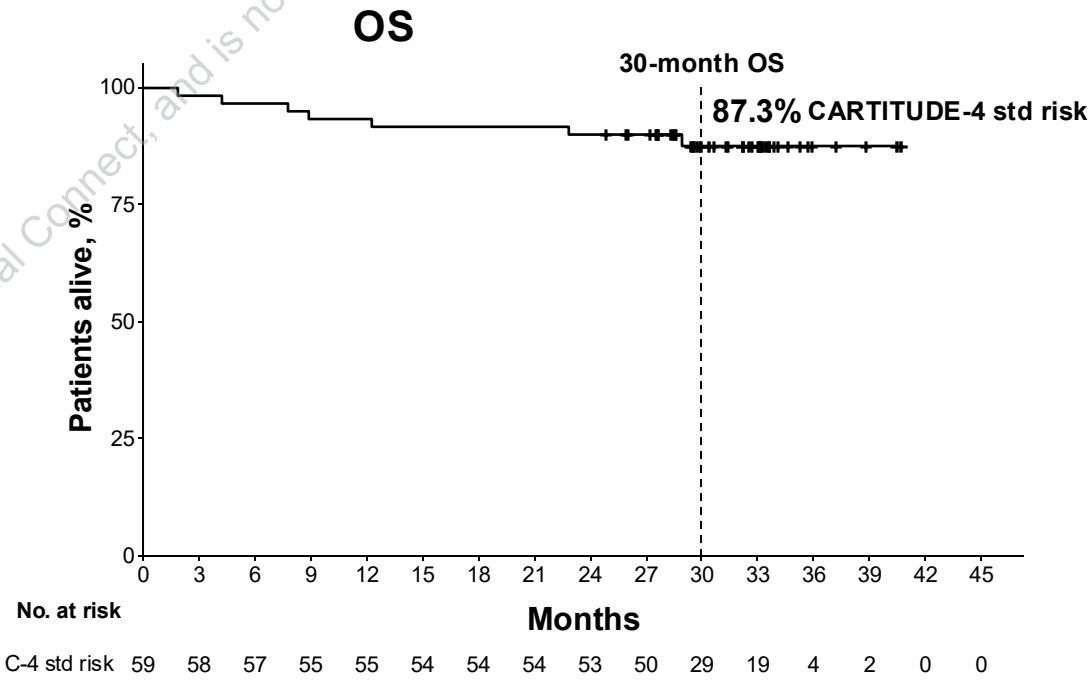
CARTITUDE-4 and CARTITUDE-1: Response Rates for Patients With Standard-Risk Cytogenetics (As-Treated)



[a]Assessed using a computerized algorithm based on IMWG consensus criteria (2016). Percentages may not add up to an exact 100% due to rounding.
IMWG, International Myeloma Working Group; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

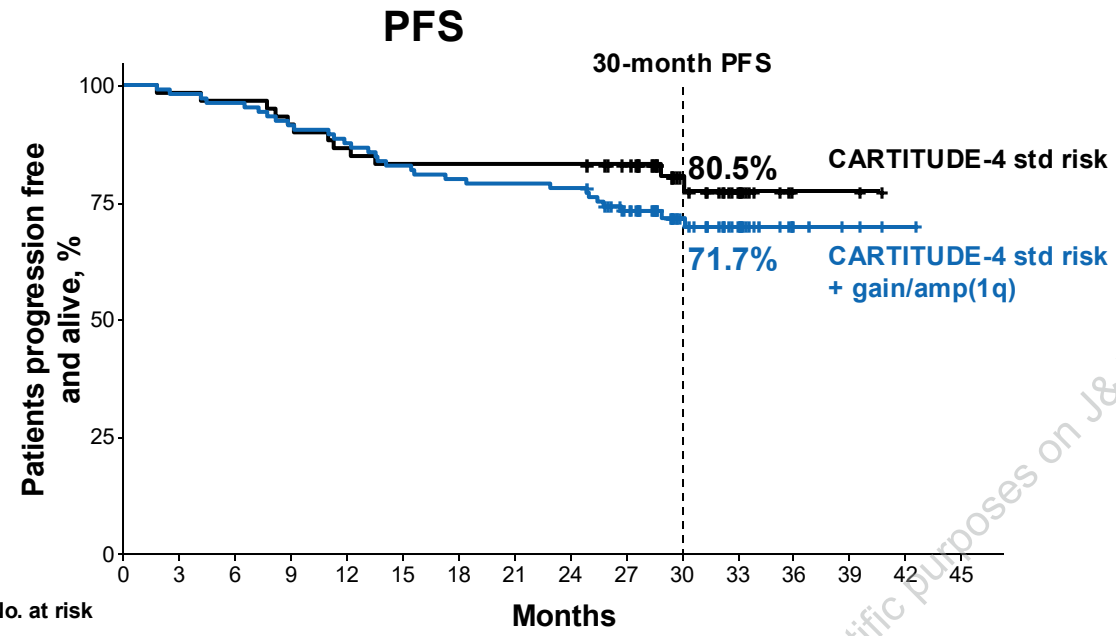
CARTITUDE-4: PFS and OS in Patients With Standard-Risk Cytogenetics (As-Treated)





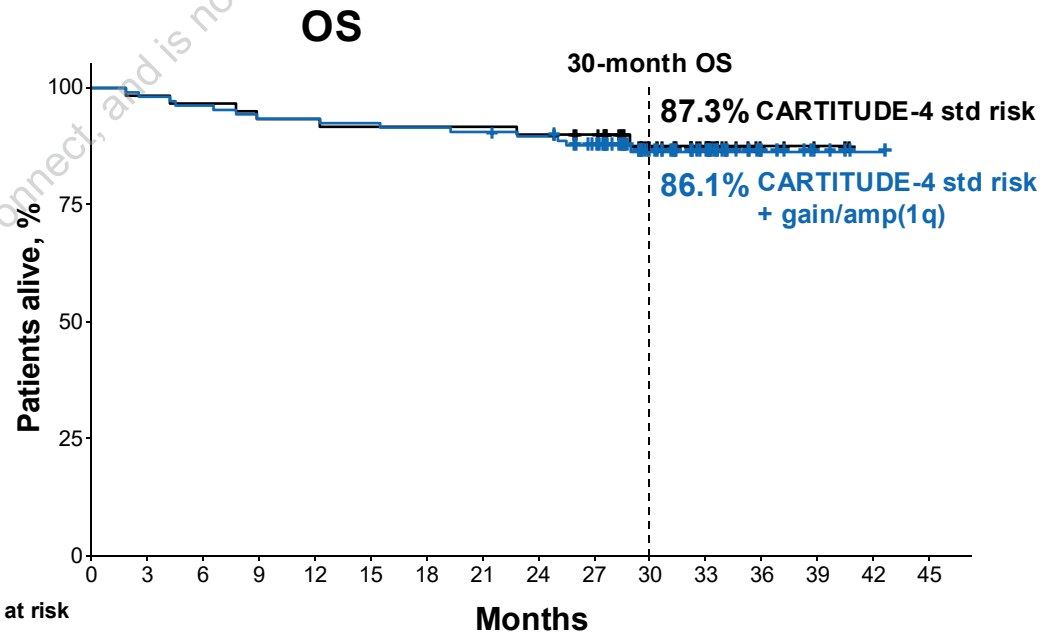
80% of CARTITUDE-4 patients with standard-risk disease who received cilta-cel as study treatment remained progression free and off treatment at 30 months

CARTITUDE-4: PFS and OS in Patients With Standard-Risk Cytogenetics (As-Treated)



No. at risk

C-4 std risk	59	58	57	54	51	49	49	49	49	45	25	15	2	2	0	0
C-4 std risk: + gain/amp(1q)	105	103	101	96	92	87	84	83	82	69	38	24	5	3	1	0



No. at risk

C-4 std risk	59	58	57	55	55	54	54	54	53	50	29	19	4	2	0	0
C-4 std risk: + gain/amp(1q)	105	103	101	98	98	97	96	95	93	86	52	34	9	4	1	0

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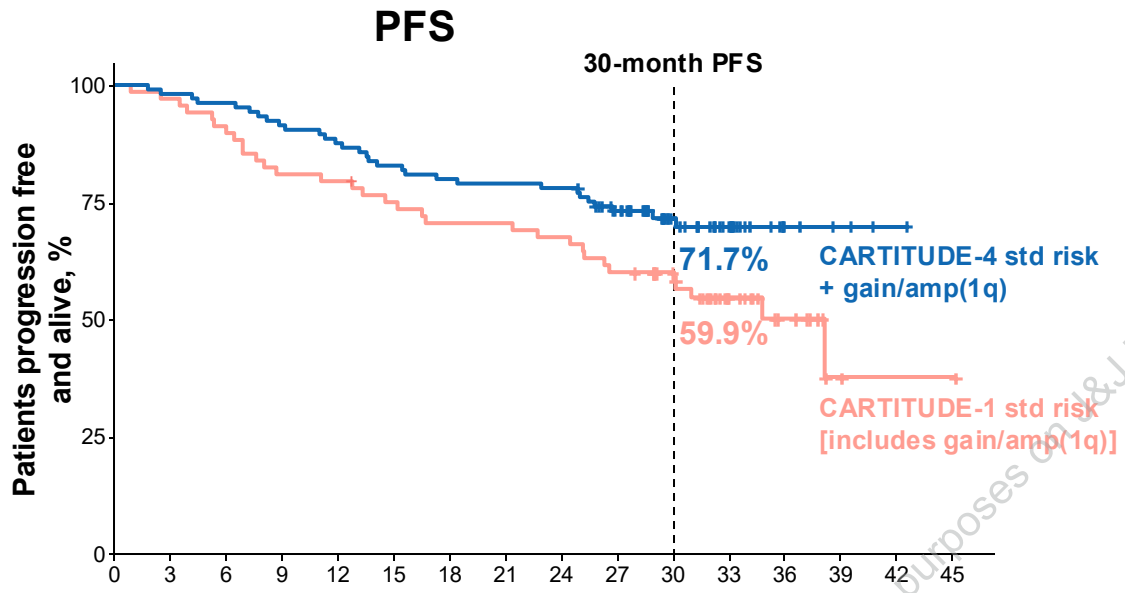
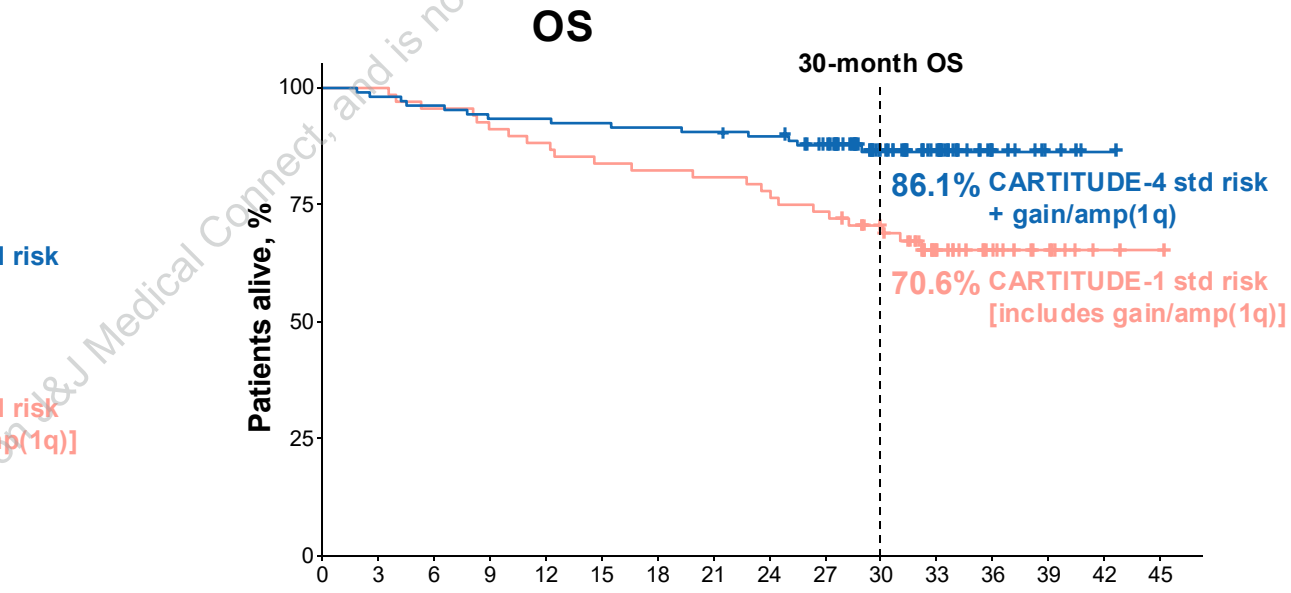
CARTITUDE-4 and CARTITUDE-1: PFS and OS in Patients With Standard-Risk Cytogenetics (As-Treated)





Survival rates were higher when cilta-cel was used earlier in standard-risk disease

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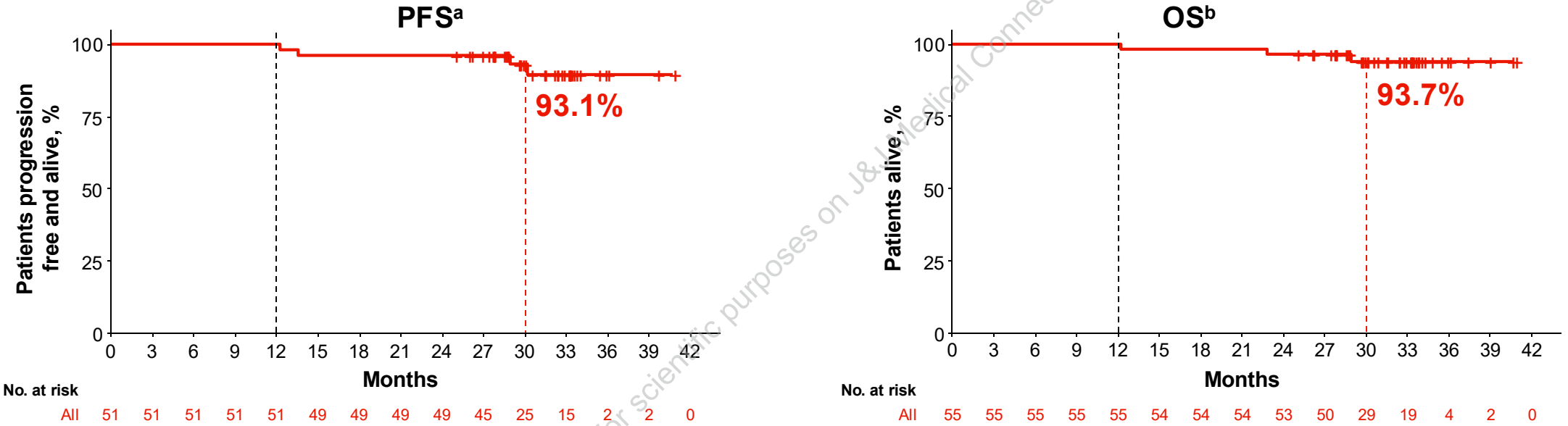
CARTITUDE-4: Survival Outcomes for Patients With Standard-Risk Cytogenetics Who Were Progression Free and Alive at 1 Year

- 86% (51/59) of patients with standard-risk cytogenetics were progression free and alive ≥1 year
  - PFS and OS rates were **~93% at 30 months** for these patients with early sustained responses



- MRD-negative CR rate at 1 year was **81%** (26/32; MRD-evaluable population at 1 year)
  - **All 26** patients remained progression free at 30 months

Treating standard-risk RRMM early with cilta-cel delivered high rates of durable remissions that extended time off treatment

[a]Includes 51 patients who were alive and progression free at 12 months. [b]Includes 55 patients alive at 12 months.

CARTITUDE-4: Safety Profile in Patients With Standard-Risk Cytogenetics

	Cilta-cel n=59
Non-hematologic SAE	31 (52.5)
Grade 3/4 infections	17 (28.8)
CRS	44 (74.6)
ICANS	1 (1.7)
CNP	4 (6.8)
IEC-parkinsonism	0

- SPMs: 8 (13.6%)
  - Cutaneous/non-invasive (n=4)
  - Non-cutaneous/invasive (n=4)
  - Hematologic (n=0)
- Non-relapse mortality: 6 (10.2%)
  - 4 deaths in first year[a]:
    - COVID-19 (n=2)
    - Subdural hematoma (n=1)
    - Multiple organ dysfunction (n=1)
  - 2 deaths beyond first year:
    - Gastric adenocarcinoma (n=1)
    - Angiosarcoma (n=1)

Safety profile of cilta-cel in standard-risk population was consistent with overall study population[1,b]

[a]From the time of cilta-cel infusion. [b]The overall cilta-cel safety population included patients from the cilta-cel arm of the CARTITUDE-4 ITT population.
CNP, cranial nerve palsy; CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; IEC, immune effector cell; SAE, serious adverse event; SPM, secondary primary malignancy.
1. Mateos M-V, et al. *Clin Lymphoma Myeloma Leuk* 2024;24(suppl 2):S290.

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Summary of Cilta-cel Outcomes in Standard-Risk Myeloma (As-Treated Population)

	30-month PFS rate, %	30-month OS rate, %
CARTITUDE-4 (median 2 prior lines)		
Cilta-cel ***Standard-risk cytogenetics per protocol***	80.5	87.3
Cilta-cel ***Standard-risk cytogenetics per protocol + gain/amp(1q)***	71.7	86.1
CARTITUDE-1 (median 6 prior lines)		
Cilta-cel ***Standard-risk cytogenetics per protocol including gain/amp(1q)***	59.9	70.6

Earlier use of cilta-cel in standard-risk RRMM led to higher survival rates

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CARTITUDE-4 Standard-Risk Disease: Conclusions

- The cilta-cel benefit-risk profile in the CARTITUDE-4 standard-risk as-treated population supports early use:
  - 80% of patients were free from progression and without treatment at 2.5 years
  - 93% of patients who were progression free at 1 year remained alive and progression-free at 2.5 years
  - Of patients in MRD-negative CR, 100% remained progression-free at 2.5 years
- Safety was consistent with the overall population
  - There were no IEC-parkinsonism events and low non-relapse mortality after 1 year in this patient population
- Earlier treatment with a single infusion of cilta-cel (CARTITUDE-4 vs CARTITUDE-1) improved survival outcomes for patients with standard-risk disease, extending time free from treatment and progression

The low rate of progression events in patients with standard-risk RRMM is indicative of a potential cure fraction, which will be further defined with additional study follow-up

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