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# 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 multiple myeloma (MM) ( $\geq 3$  prior lines of therapy [LOT]) were treatment and progression free for  $\geq 5$  years after a single infusion, providing the first evidence that ciltacabtagene autoleucel (cilta-cel) is potentially curative in relapsed/refractory multiple myeloma (RRMM)<sup>1</sup>
- Across a median follow-up of 33.6 months, cilta-cel significantly improved progression-free survival (PFS) and overall survival (OS) vs standard of care (SOC) in the earlier-line RRMM population in CARTITUDE-4<sup>2,3</sup>
  - 30-month OS was 76.4% for cilta-cel vs 63.8% for SOC in the intent-to-treat (ITT) analysis (hazard ratio [HR], 0.55; 95% CI, 1.58–3.55;  $P < 0.0001$ )<sup>3</sup>
  - PFS and OS benefits vs SOC were consistent in patients with high-risk cytogenetics<sup>3</sup> and functionally high-risk patients<sup>4</sup>
- Patients with standard-risk RRMM<sup>5,6</sup> and patients with early sustained minimal residual disease (MRD) response<sup>7</sup> may have the highest likelihood of cure
- Here, we report outcomes in CARTITUDE-4 patients with standard-risk cytogenetics<sup>5</sup>

## METHODS

Figure 1: CARTITUDE-4 study design<sup>2</sup>

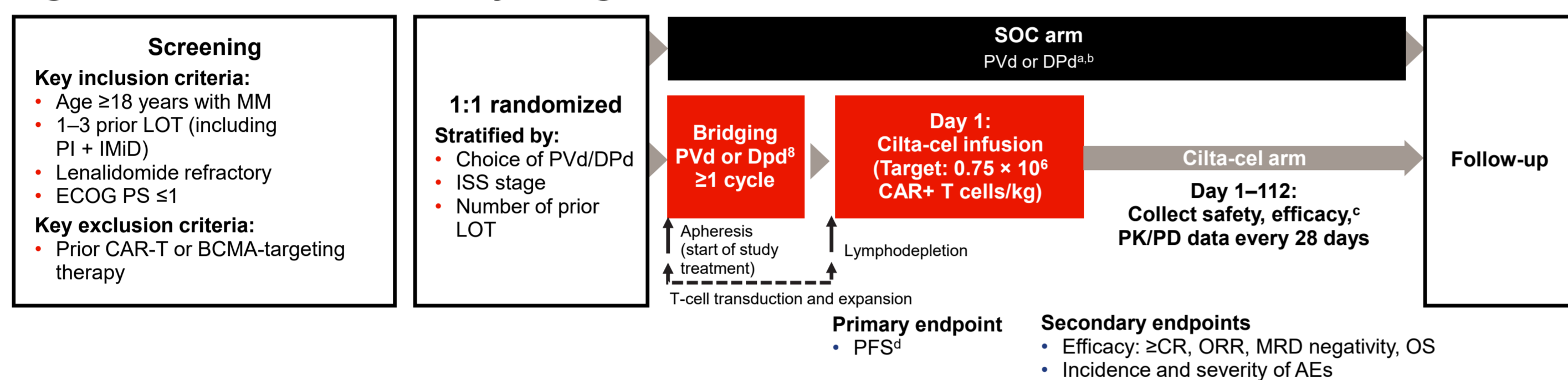
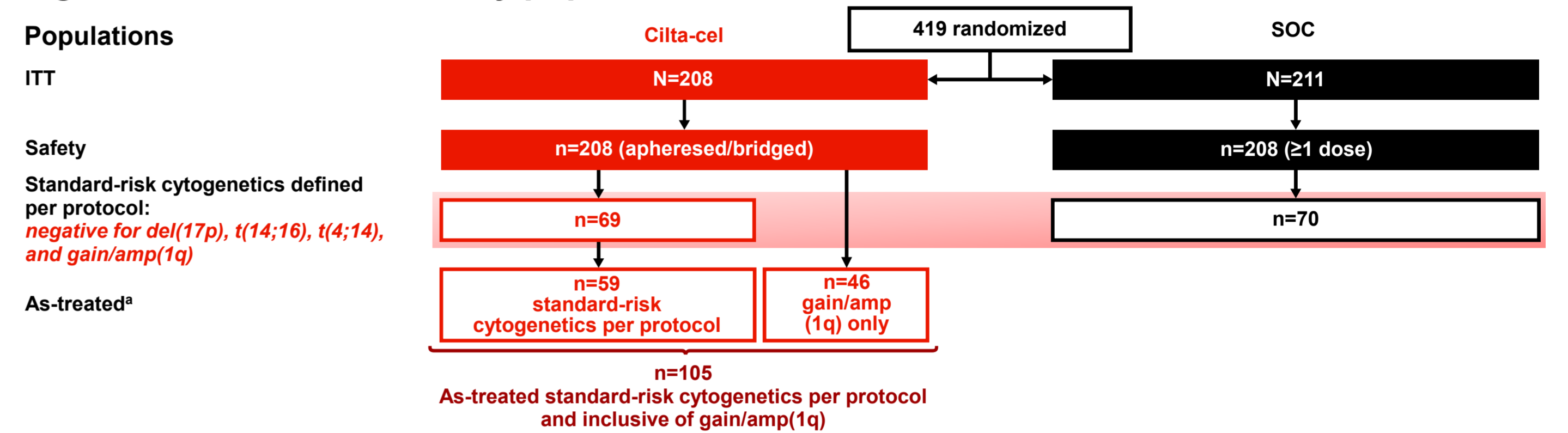


Figure 2: CARTITUDE-4 study population



## RESULTS

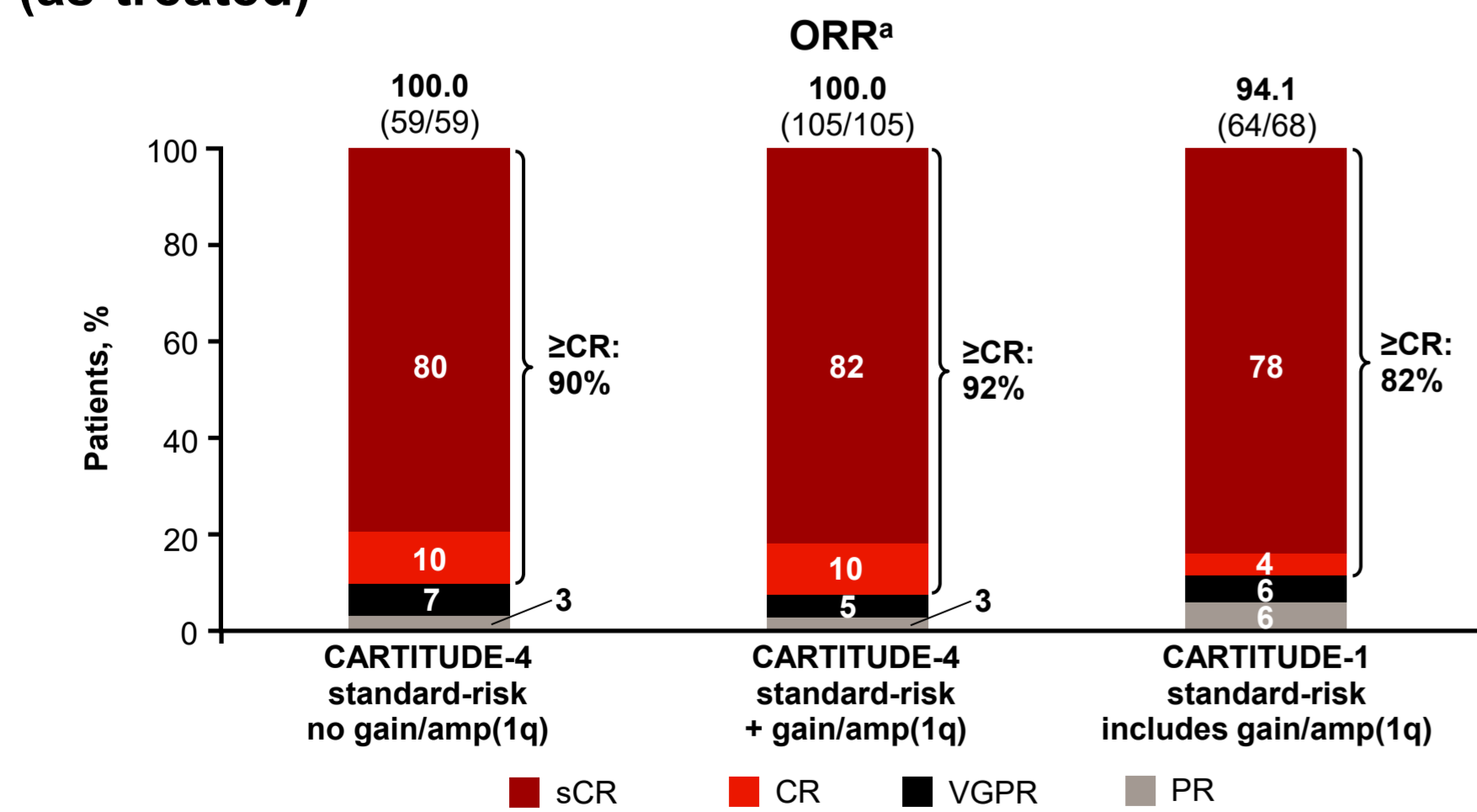
- In CARTITUDE-4, cilta-cel improved PFS and OS in the ITT population with standard- and high-risk cytogenetics<sup>5</sup>
  - For standard-risk patients, the 30-month PFS rate was 71.0% with cilta-cel and 43.2% with SOC; 30-month OS rates were 79.7% and 75.5%, respectively
- For high-risk patients, the 30-month PFS rate was 52.3% with cilta-cel and 17.5% with SOC; 30-month OS rates were 75.5% and 62.1%, respectively
- Baseline characteristics were similar between the groups (Table 1)

Table 1: Baseline characteristics of CARTITUDE-1 and CARTITUDE-4 patients with standard-risk cytogenetics

Baseline characteristics	CARTITUDE-4 standard-risk cytogenetics (as-treated)		CARTITUDE-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 LOT, n (%)			
1	20 (33.9)	33 (31.4)	0
2	22 (37.3)	42 (40.0)	0
3	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)

- Treating standard-risk disease with cilta-cel elicited response rates between 94.1% and 100%; a large majority of these were complete responses (Figure 3)

Figure 3: Response rates of CARTITUDE-1 and CARTITUDE-4 patients with standard-risk cytogenetics (as-treated)



- OS and PFS remained high in standard-risk patients across 30 months of follow-up, even when including those with gain/amp(1q) (Figure 4)
- Survival rates were higher when cilta-cel was used earlier in standard-risk disease (Figure 5)

Figure 4: PFS (A) and OS (B) in CARTITUDE-4 patients with standard-risk cytogenetics (as-treated)

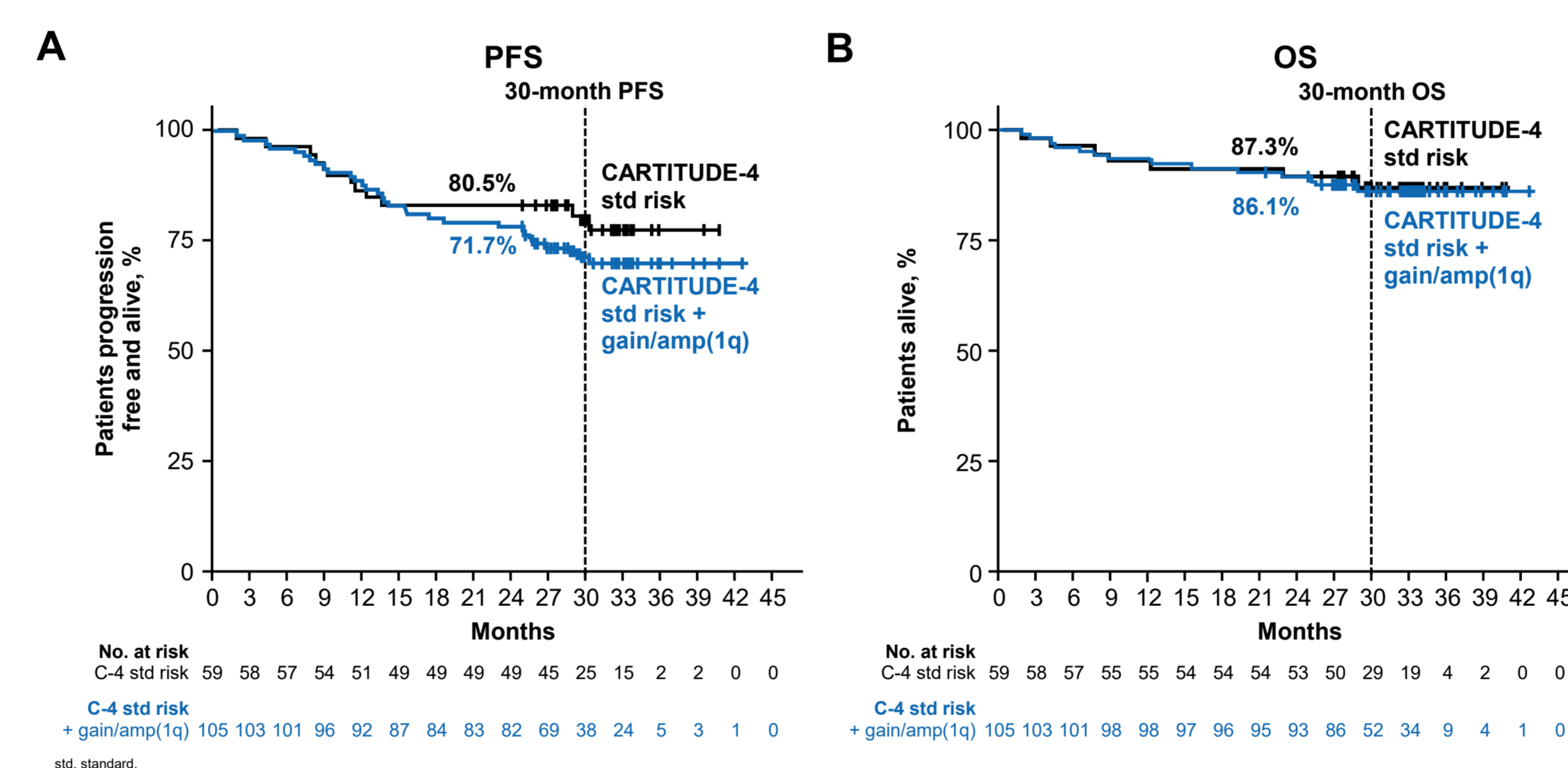
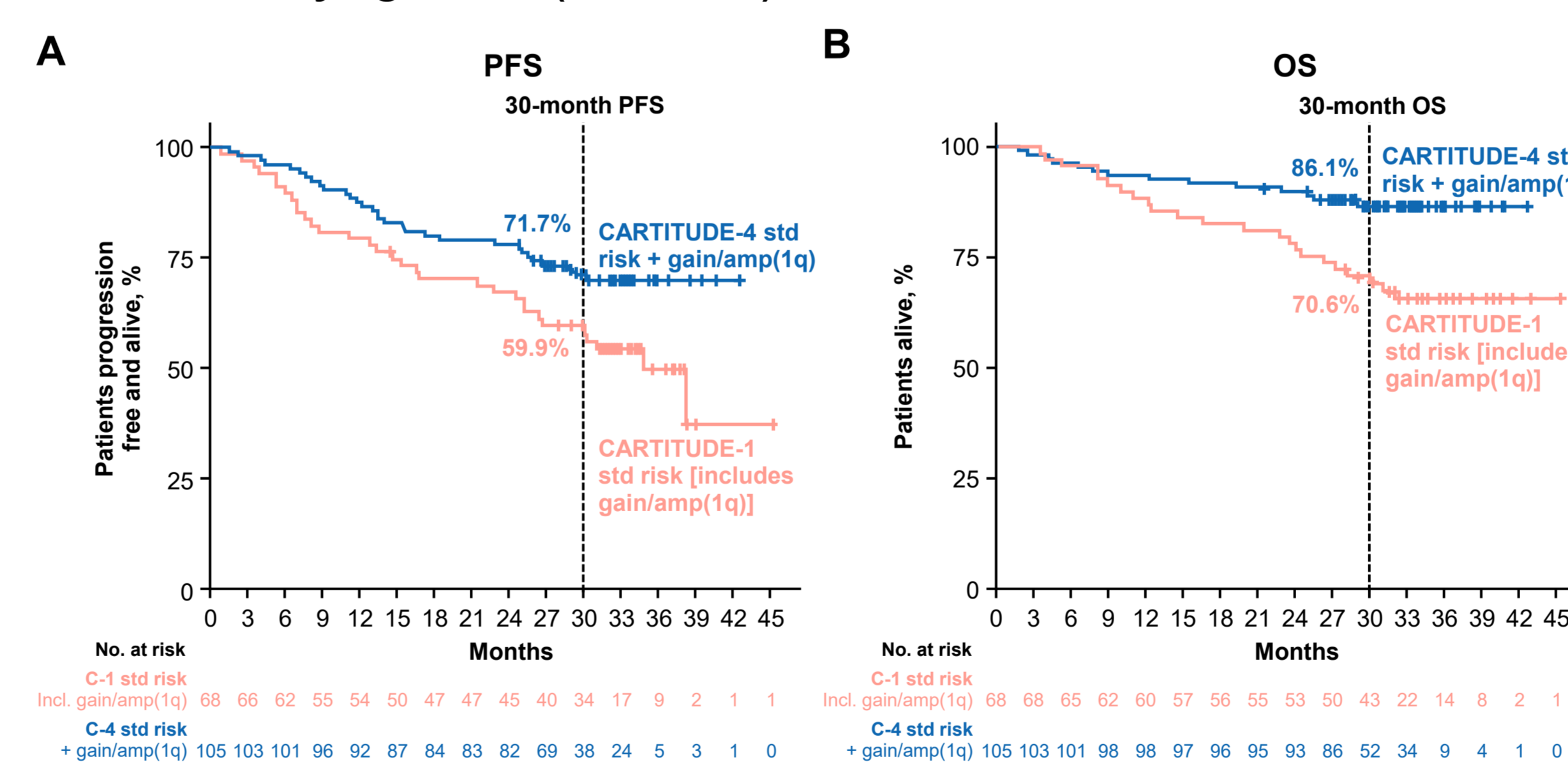


Figure 5: PFS (A) and OS (B) in CARTITUDE-1 and CARTITUDE-4 patients with standard-risk cytogenetics (as-treated)



- Treating standard-risk RRMM early with cilta-cel delivered high rates of durable remissions that extended time off treatment
- 86% (51/59) of patients with standard-risk cytogenetics were progression free and alive  $\geq 1$  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
- Safety profile of cilta-cel in standard-risk population was consistent with overall study population (Table 2)<sup>3</sup>
  - 8 (13.6%) patients were diagnosed with a secondary primary malignancy
  - 6 (10.2%) patients died without prior relapse or progression

Table 2: Safety in CARTITUDE-4 patients with standard-risk cytogenetics<sup>a</sup>

	Cilta-cel (n=59)
Nonhematologic 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

a: 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.

## CONCLUSION

### Key Takeaway

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

### Conclusions

- 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
- Safety was consistent with the overall population

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