Full title: Dose Optimization of Elranatamab to Mitigate the Risk of Cytokine Release Syndrome in Patients With Multiple Myeloma

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Supplementary Information

Supplemental Table 1. Clinical trials included in the CRS analysis.

Clinical trial	**Phase**	**Population**	**Dosing regimen**	**Priming/premedication regimens**	**CRS/ICANS grading criteria**
MagnetisMM-1 (NCT03269136)	1	Patients with RRMM	Dose escalation: elranatamab IV 0.1-50 µg/kg QW or SC 80-1000 µg/kg QW	No step-up priming doses or premedication for CRS[a]	ASTCT (except for CRS in the IV cohort where

			Elranatamab SC 1000 µg/kg or 76 mg QW	Single priming dose of 600[b] µg/kg or 44 mg administered with or without premedication[c]	Lee et al. 2014 criteria were used)
MagnetisMM-2 (NCT04798586)	1	Japanese patients with RRMM	Elranatamab SC 1000 µg/kg QW	Single priming dose of 600[b] µg/kg administered with premedication[c]	ASTCT
MagnetisMM-3 (NCT04649359)	2	Patients with RRMM naïve to or who previously received BCMA-directed therapies	Elranatamab SC 76 mg QW	12/32 mg priming doses on Day 1 and Day 4, respectively, with premedication[c] for CRS	ASTCT
MagnetisMM-9 (NCT05014412)	1/2	Patients with RRMM	Elranatamab SC 76 mg QW[d]	4/20 mg priming doses on Day 1 and Day 4,	ASTCT

				respectively, with premedication[c] for CRS	

[a] One patient each in the SC 600 µg/kg (n=6) and 1000 µg/kg (n=6) cohorts received premedication for CRS. [b] 600/1000 µg/kg is the body weight–based equivalent of 44/76 mg for a 75-kg patient. [c] Premedication for CRS included 650 mg of acetaminophen or 500 mg of paracetamol, 25 mg of diphenhydramine, and 20 mg of dexamethasone or equivalent. [d] In some cohorts of MagnetisMM-9, higher doses were administered starting at cycle 2; therefore, only the first 4 doses were included in this analysis in order to rule out any impact of higher doses on CRS.

ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; IV, intravenous; QW, once weekly; SC, subcutaneous; RRMM, relapsed or refractory multiple myeloma.

Supplemental Table 2. Models for any-grade and grade ≥2 CRS vs elranatamab exposure in MagnetisMM-1.

CRS endpoint	**Effects**	**Estimate (95% CI)**	**Odds ratio (95% CI)**	**Pr(>|Z|)**
Any-grade CRS	Intercept	−6.1341 (−10.4 to −3.0)	–	0.001
	Log ($C_{max,24h}$), ng/mL	1.2985 (0.74 to 2.1)	3.7 (2.1-7.9)	<0.001
Grade ≥2 CRS	Intercept	−5.4 (−9.1 to −2.6)	–	0.001

CRS endpoint	Effects	Estimate (95% CI)	Odds ratio (95% CI)	Pr(>|Z|)
	Log ($C_{max,24h}$), ng/mL	0.75 (0.3 to 1.3)	2.1 (1.4-3.7)	0.004

C_{max}, maximum serum concentration; CRS, cytokine release syndrome.

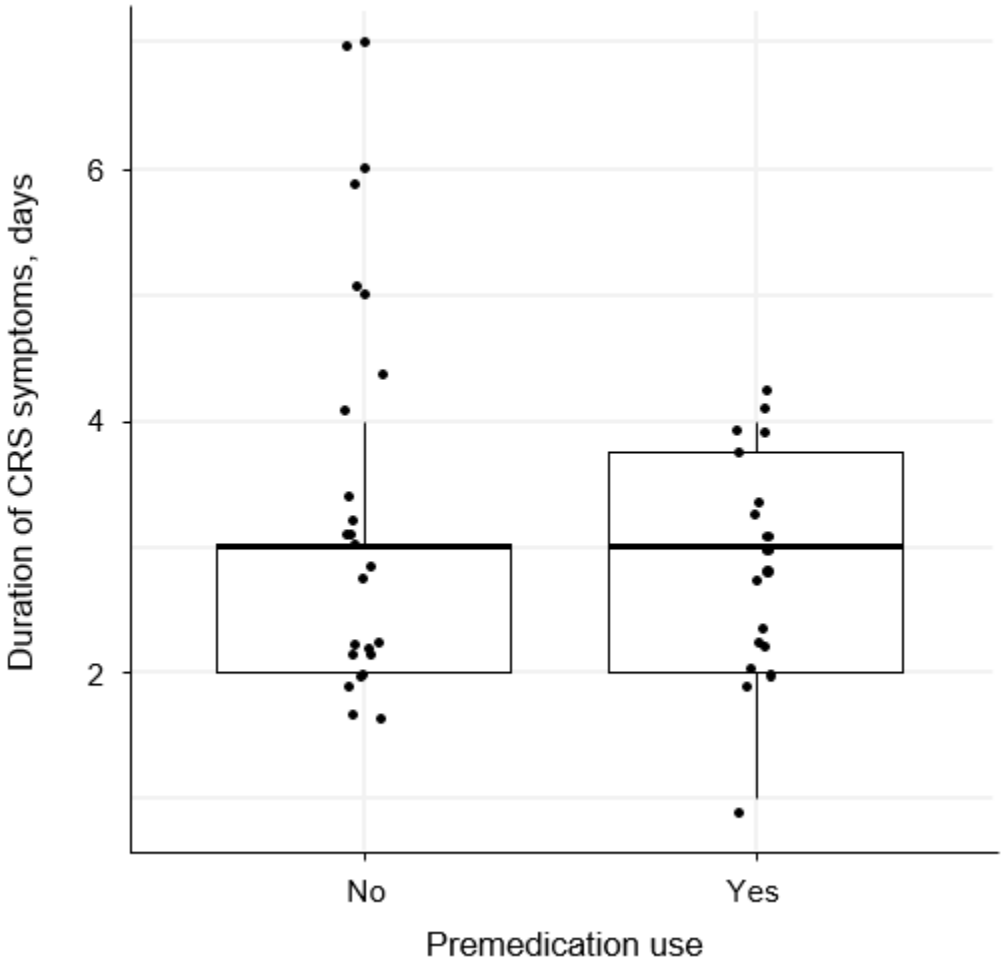
Supplemental Table 3. Predicted and observed incidences of any-grade and grade ≥2 CRS at different starting dose levels

CRS incidence	**4 mg**	**12 mg**	**44 mg**
Predicted CRS rate, median (95% CI), %			
Any-grade CRS	40.7 (20.9-63.9)	60.1 (42.7-75.2)	93.4 (83.3-97.6)
Grade ≥2 CRS	11.1 (4.0-27.3)	16.3 (7.8-31.2)	41.6 (29.4-54.9)
Observed CRS rate, %			
Any-grade CRS	63.5	57.9	100.0[a]/78.3[b]
Grade ≥2 CRS	15.3	14.2	50.0[a]/47.8[b]

[a] Refers to observed CRS rates for patients who received the 44/76 mg regimen without premedication. [b] Refers to observed CRS rates for patients who received the 44/76 mg regimen with premedication.

CRS, cytokine release syndrome.

Supplemental Figure 1. Duration of CRS in patients who received the 1-step-up dose single priming regimen with or without premedication.



CRS, cytokine release syndrome.