Running title: Elranatamab Exposure-Response Efficacy Analysis

Full title: Population Exposure-Response Efficacy Analysis of Elranatamab (PF-06863135) in Patients with Multiple Myeloma

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Supplementary Information

Supplemental Figure 1. Free Elranatamab Exposure By Complete Response and Baseline sBCMA Levels

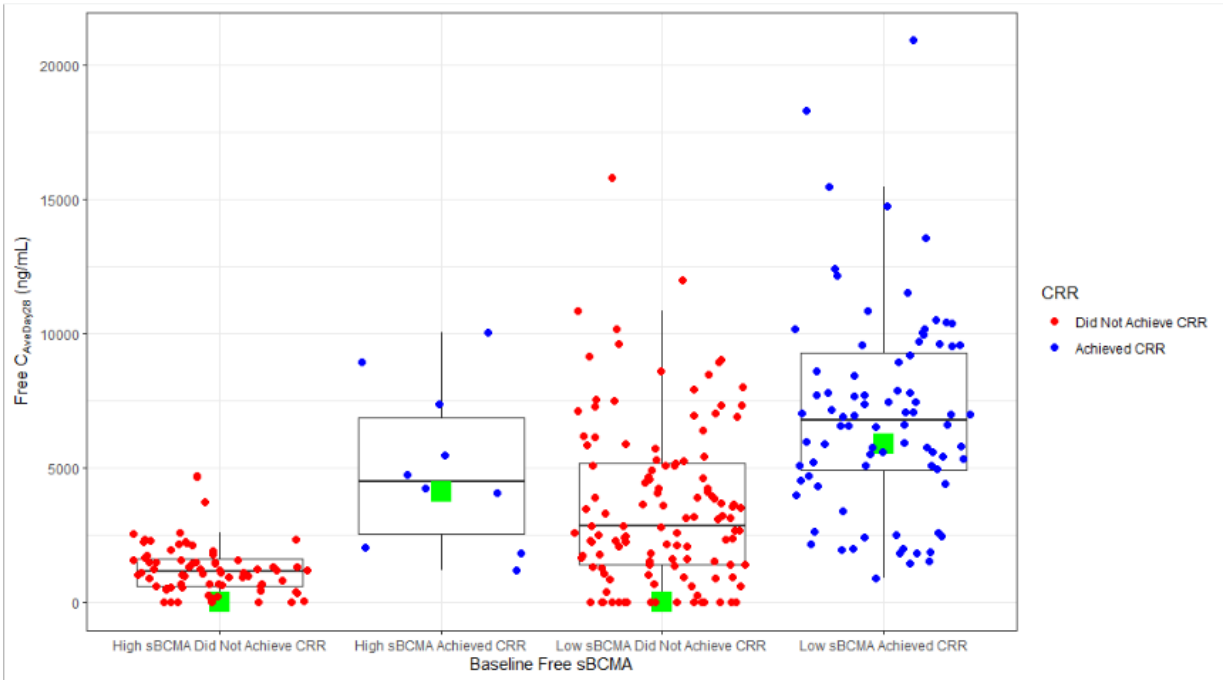
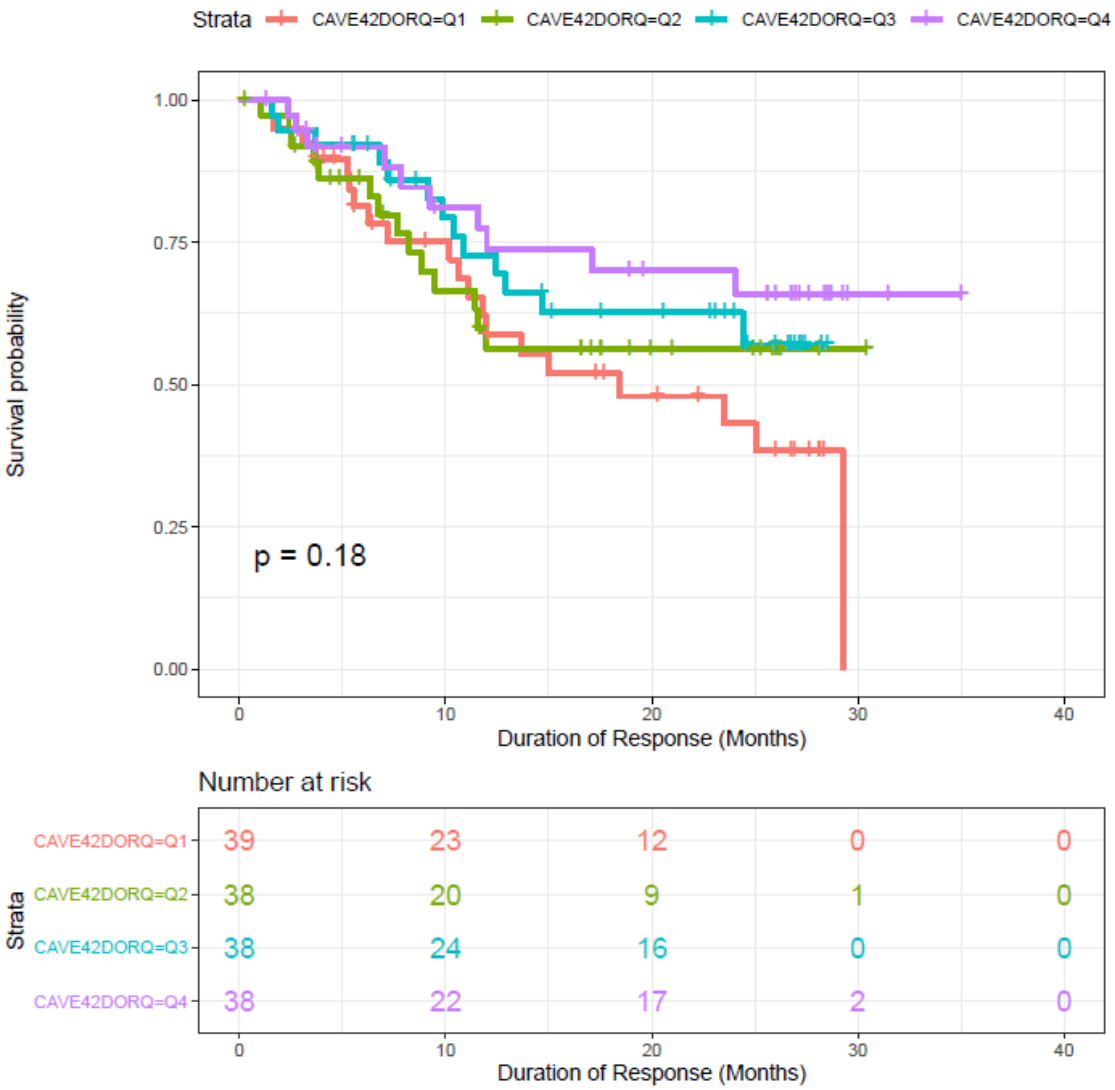


Figure 1. Green squares represent the geometric mean of elranatamab concentration on Day 28 the corresponding group. Patients with baseline sBCMA concentration of equal to or more than 100 ng/mL were categorized as “High sBCMA” patients, and patients with less than 100 ng/mL baseline sBCMA concentration were in the “Low sBCMA” group.

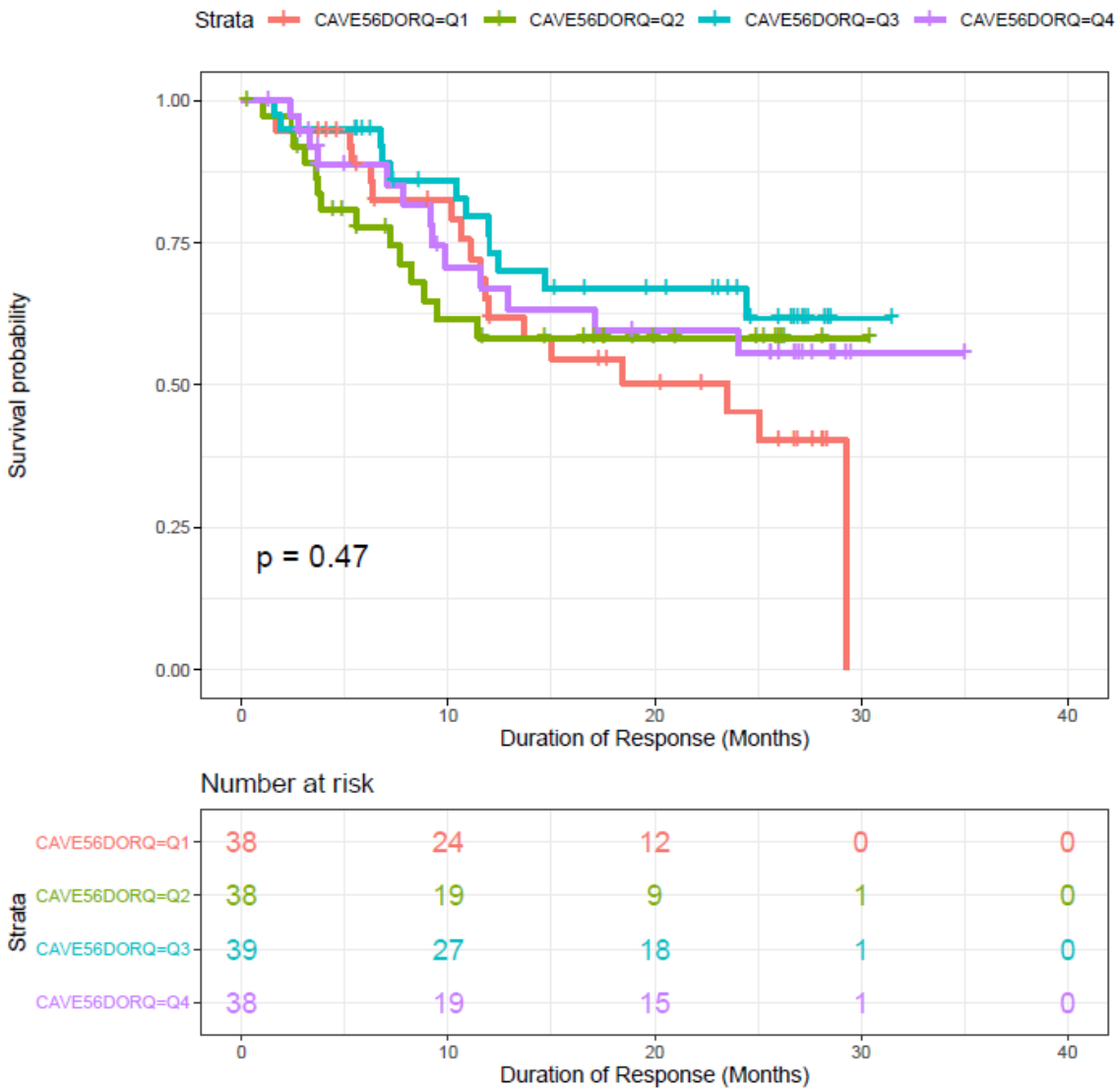
Abbreviations: CRR = Complete Response Rate; BCMA = B-cell Maturation Antigen.

Supplemental Figure 2. Kaplan-Meier Curves for DOR

A. Stratified By Predicted $C_{ave,\ Day\ 42}$ Quartiles



B. Stratified By Predicted $C_{ave,\ Day\ 56}$ Quartiles



C. Stratified By Predicted $C_{ave,\ Day\ 70}$ Quartiles

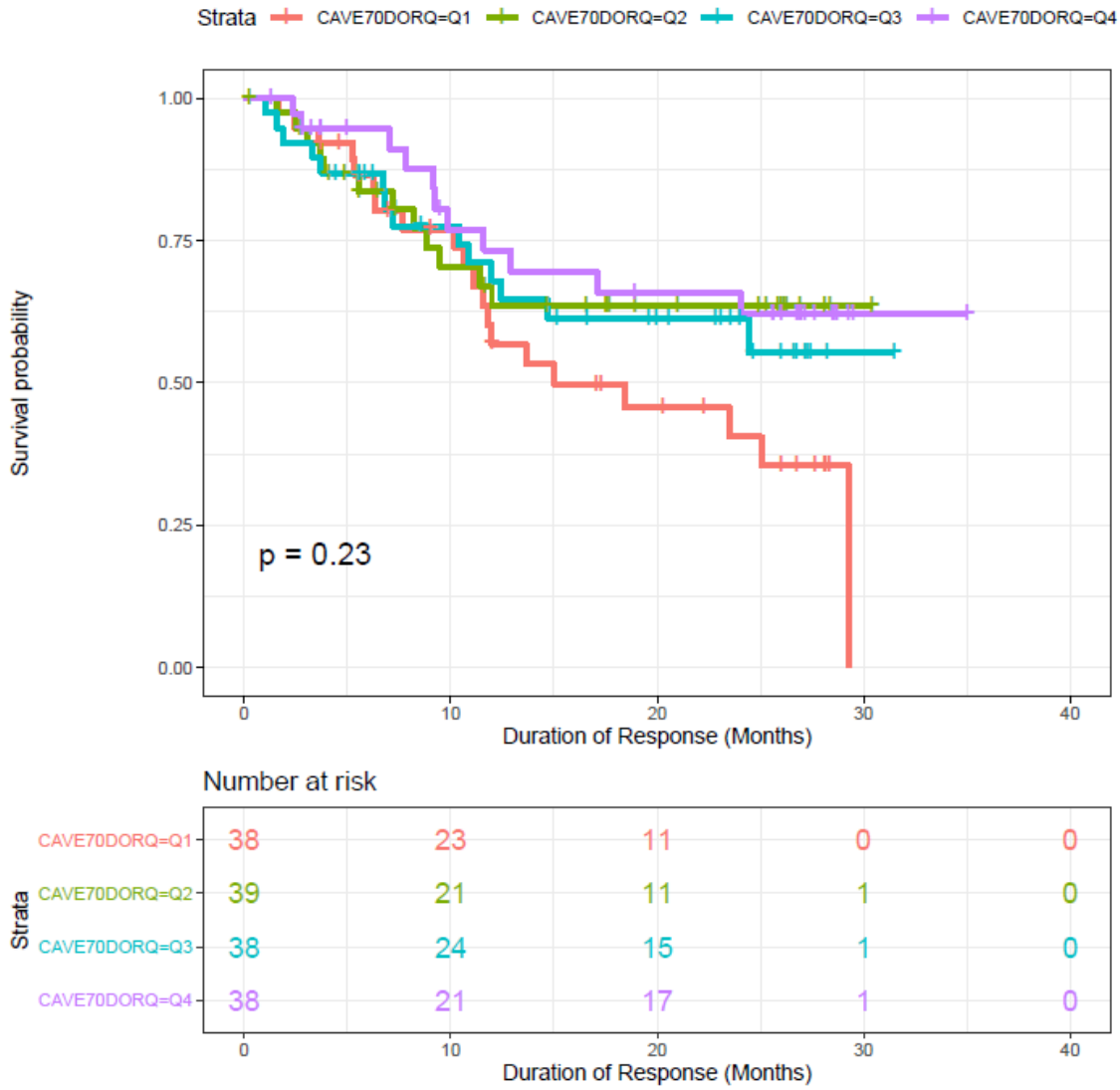
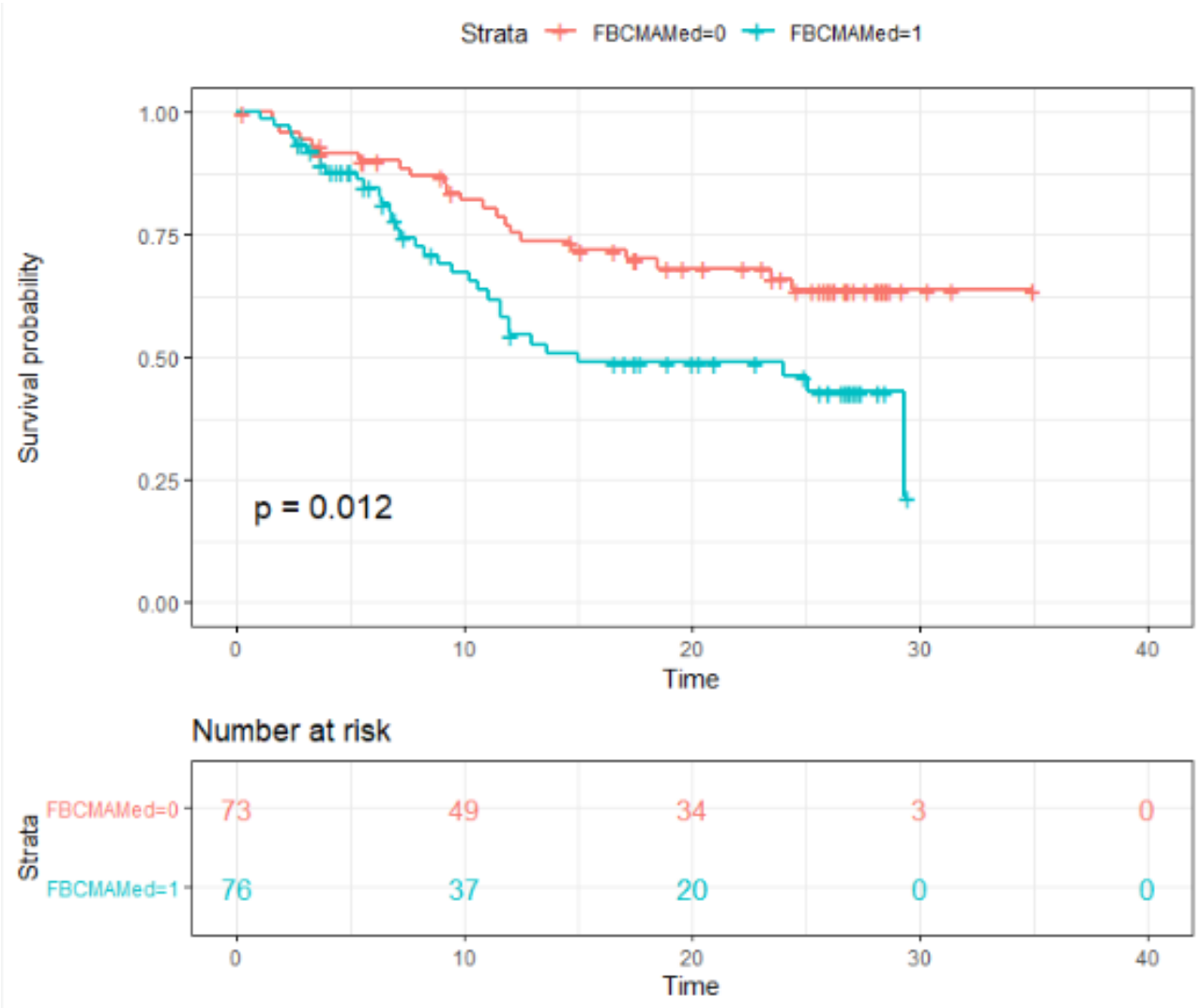


Figure 2: Figure 2A, 2B, and 2C show the Kaplan-Meier curves for DOR Stratified by predicted $C_{ave,Day42}$, $C_{ave,Day56,}$ and $C_{ave,Day70}$ quartiles, respectively. Q1, Q2, Q3, and Q4 indicate the group of patients with elranatamab exposure below the first quartile, between the first quartile and the median, between the median and the third quartile, and above the third quartile, respectively.

Abbreviations: DOR = Duration of Response Rate

Supplemental Figure 3. Kaplan-Meier Curves for DOR

A. Stratified By Median sBCMA at Baseline



B. By Disease Stage R-ISS

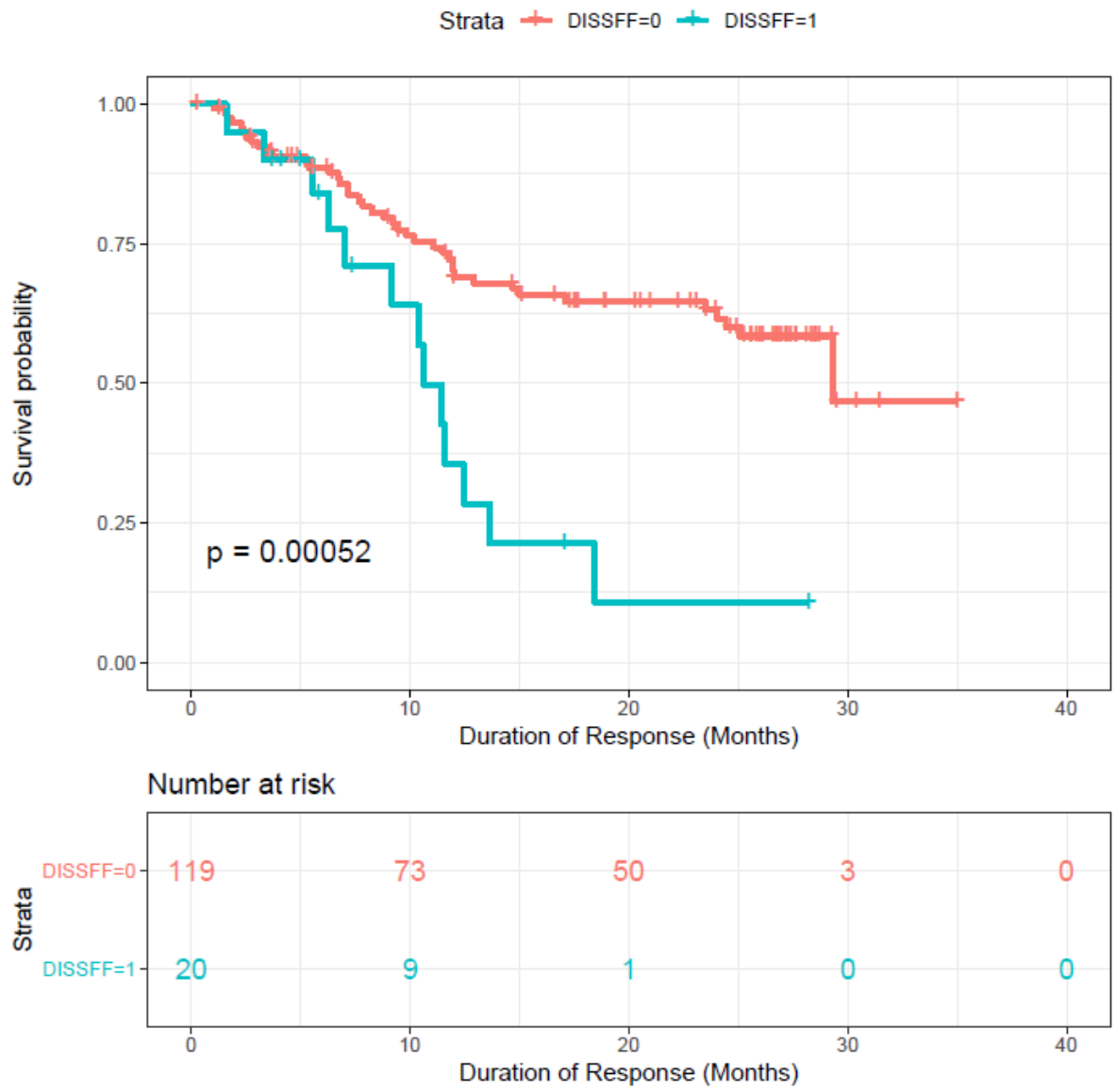


Figure 3: Figure 3A and 3B show the Kaplan-Meier curves for DOR Stratified by predicted median baseline sBCMA and by disease stage R-ISS, respectively. In Figure 3A, FBCMAMed=0 and FBCMAMed=1 indicate the group of patients with baseline sBCMA below and equal to or above the median, respectively. In Figure 3B, DISSFF=0 indicates the group of patients with R-ISS of 1 or 2; DISSFF=1 indicates the group of patients with R-ISS of 3.

Abbreviations: DOR = Duration of Response Rate; BCMA = B-cell Maturation Antigen: DISS = disease stage status

Supplemental Table 1. Covariates Evaluated

Covariate Type	Description
Continuous	Age Baseline body weight Baseline creatinine clearance. Baseline free sBCMA Baseline platelet count
Categorical	Sex Race (White or others, and Asian or others) Extramedullary disease status Type of myeloma (IgG, or non-IgG/Light chain only) % Bone marrow plasma cells (< 70 % or ≥ 70 %) Baseline cytogenetics (high or standard) Prior stem cell transplant Disease stage R-ISS (1-2 or 3) Whether participant was refractory to last therapy Penta-refractory status ECOG performance status (0/1 or 2/3) Number of prior lines of therapy (> 5 or <= 5) ADAB status ADAT status Tumor burden (high or others)* Prior BCMA therapy

Abbreviations: ADAB=negative or positive anti-drug-antibody (ADA) status at baseline; ADAT=negative or positive anti-drug-antibody (ADA) status; an ADA-positive subject is defined as a subject with ≥ 1 treatment-induced or treatment-boosted ADA response; ECOG=Eastern Cooperative Oncology Group; R-ISS = Revised International Staging System; sBCMA= soluble B-cell Maturation Antigen.
*For tumor burden, a participant was defined to have high tumor burden at baseline if: plasma cell infiltrate in the
bone marrow ≥ 80 % or serum M-spkie ≥ 5 g/dL or serum free light chain ≥ 5000 mg/L. Missing tumor burden was assigned if any or all of the these lab value was missing. Patients who did not fit either criterion were categorized as having low/intermediate tumor burden (others). Prior BCMA therapy indicated whether a participant had received prior BCMA-directed antibody-drug conjugate (ADC) or BCMA-directed chimeric antigen receptor T-cell therapy (CAR-T)-cell therapy, either approved or investigational.

Supplemental Table 2. Patient demographics and baseline characteristics

	MagnetisMM-1 **n=88**	**MagnetisMM-2** **n=4**	**MagnetisMM-3** **n=187**	**MagnetisMM-9** **n=33**	**Total** **n=312**
Median age (range), years	65.0 (42, 82)	68.5 (49, 70)	68.0 (36, 89)	63.0 (36, 79)	66.0 (36, 89)
Sex, n (%)					

Male	45 (51)	3 (75)	98 (52)	14 (42)	160 (51)
Female	43 (49)	1 (25)	85 (48)	19 (58)	152 (49)
Race, n (%)					
White	61 (69%)	0	116 (62%)	11 (33%)	188 (60%)
Black/African American	16 (18%)	0	11 (6%)	2 (6%)	29 (9%)
Asian	6 (7%)	4 (100%)	17 (9%)	19 (58%)	46 (15%)
Missing/Unknown	5 (6%)	0	43 (23%)	1 (3%)	49 (16%)
Median baseline body weight (range), kg	72.1 (42.0, 121.9)	70.1 (61.4, 73.5)	71.8 (36.5, 159.6)	66.3 (44.5, 101.5)	71.4 (36.5, 159.6)
Median baseline sBCMA* (range) (n) (ng/mL)	33.0 (0.08, 598) (74)	53.0 (22, 76) (4)	48.3 (0.27, 606) (176)	41.8 (2.37, 336) (33)	44.4 (0.08, 606) (298)
ECOG PS, n (%)					
0/1	79 (90%)	4 (100%)	176 (94%)	33 (100%)	292 (94%)
2/3	9 (10%)	0 (0%)	11 (6%)	0 (0%)	20 (6%)
Derived disease stage (ISS), n (%)					
I/II	57 (65%)	3 (75)	143 (76%)	23 (70%)	226 (72%)
III	21 (24%)	1 (25)	34 (18%)	7 (21%)	63 (20%)
Missing/Unknown	10 (11%)	0	10 (5%)	3 (9%)	23 (7%)

Cytogenetic risk, n (%)					
Standard	54 (61%)	3 (75)	125 (67%)	23 (70%)	205 (66%)
High-Risk	26 (30%)	1 (25)	44 (24%)	10 (30%)	81 (26%)
Missing/Unknown	8 (9%)	0	18 (10%)	0 (0%)	26 (8%)
Extramedullary disease based on investigator, n (%)					
Yes	20 (23%)	2 (50%)	74 (40%)	13 (39%)	109 (35%)
Missing/Unknown	36 (41%)	0 (0)	0 (0)	0 (0)	36 (12%)
Number of prior lines of therapy ≥ 5, n (%)	48 (55%)	4 (100%)	91 (49%)	16 (48%)	159 (51%)
Prior BCMA-directed therapy, n (%)	22 (25%)	1 (25%)	64 (34%)	9 (27%)	96 (31%)

*Summary is based on subjects with baseline sBCMA values available

Abbreviations: BCMA = B-cell maturation antigen; ECOG PS = Eastern Cooperative Oncology Group performance status; R-ISS = revised International Staging System.

Supplemental Table 3. Model for ORR vs Elranatamab Exposure Metric $C_{ave, Event}$

Endpoint	Effects	Estimate (95% CIs)	Odds Ratio (95% CIs)	Pr(>|Z|)
ORR	Intercept	-13.5 (-17.5 - -10.1)	-	< 0.001
	Log free ($C_{ave, Event}$) (ng/mL)	4.09 (3.12 – 5.21)	59.54 (22.58 – 182.6)	< 0.001
	With EMD at Baseline	-1.18 (-1.92 – -0.471)	0.3066 (0.1462 – 0.6246)	0.0013
	With Prior BCMA Therapy	-1.01 (-1.79 - -0.267)	0.3628 (0.1676 - 0.7656)	0.0086
N = 299				

Abbreviations: ORR = Objective Response Rate; BCMA = B-cell Maturation Antigen; EMD = extramedullary disease; CIs = Confidence Intervals

Supplemental Table 4. Model for CRR vs Elranatamab Exposure Metric $C_{ave, Event}$

Endpoint	Effects	Estimate (95% CIs)	Odds Ratio (95% CIs)	Pr(>|Z|)
CRR	Intercept	-11 (-14.7 – -7.73)	-	< 0.001
	Log free ($C_{ave, Event}$) (ng/mL)	2.86 (2.01 – 3.85)	17.5 (7.437 – 46.88)	< 0.001
	With EMD at Baseline	-1.61 (-2.38 – -0.902)	0.1994 (0.09267 - 0.4057)	< 0.001
	"Light chain only" as Type of Myeloma	1.2 (0.445 – 2)	3.329 (1.561 – 7.378)	0.0023
N = 299				

Abbreviations: CRR = Complete Response Rate; EMD = extramedullary disease; CIs = Confidence Intervals