

Elranatamab Fixed Dosing: The Optimal Dosing Strategy for Safety, Efficacy, and Convenience Across Body Weights

Objectives



To evaluate the impact of body weight (BW) on the pharmacokinetics (PK), safety, and efficacy of fixed dosing of elranatamab in patients with relapsed/refractory multiple myeloma (RRMM)

Conclusions



- Concerns with flat dosing include the potential for overdosing patients with lower BW and underdosing individuals with higher BW
- However, this study provides evidence that fixed dosing of elranatamab is effective and has a consistent and manageable safety profile across a broad range of BWs
- BW has no significant impact on the PK, safety, or efficacy of elranatamab
- These findings support the approved fixed dosing of elranatamab in patients with RRMM



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References: 1. Klein C, et al. Nat Rev Drug Discov. 2024;23:301-319. 2. Elrexfio (elranatamab-bcmm). Prescribing information. Pfizer; 2023. 3. Elrexfio (elranatamab-bcmm). Summary of product characteristics. Pfizer Europe MA EEIG; 2023. 4. Japan Pharmaceuticals and Medical Devices Agency. Accessed May 12, 2025. <https://www.pmda.go.jp/files/000274881.pdf>. 5. Lesokhin A et al. Nat Med 2023;29:2259-2267.

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Background

- Bispecific T-cell engagers (TCEs) are a promising modality for cancer treatment,¹ and evaluation of dosing strategies, including utilization of BW-based versus fixed dosing, is essential to ensure optimal therapeutic outcomes
- Elranatamab is a bispecific TCE that targets B-cell maturation antigen (BCMA) on myeloma cells and CD3 on T cells²
 - Elranatamab is approved for the treatment of adult patients with RRMM²⁻⁴
- Here, we provide data evaluating the impact of BW on the PK, safety, and efficacy of elranatamab, supporting the approved fixed dosing strategy for elranatamab

Results

PATIENTS

- 187 patients (both cohorts) were enrolled in MagnetisMM-3
- Baseline characteristics were balanced across quartiles (**Table 1**)

Table 1. Baseline patient characteristics by BW quartile

Characteristic	Quartile 1 (n=47)	Quartile 2 (n=48)	Quartile 3 (n=48)	Quartile 4 (n=45)
Median age (range), years	70 (36-84)	71 (48-85)	66 (41-88)	65 (46-78)
Female, n (%)	28 (59.6)	33 (68.8)	17 (39.5)	10 (22.2)
Race, n (%)				
White	23 (48.9)	28 (58.3)	27 (62.8)	34 (75.6)
Asian	9 (19.1)	3 (6.3)	4 (9.3)	1 (2.2)
Black or African American	2 (4.3)	3 (6.3)	3 (7.0)	3 (6.7)
Not reported or unknown	13 (27.7)	14 (29.2)	9 (20.9)	7 (15.6)
ECOG performance status, n (%)				
0	16 (34.0)	18 (37.5)	19 (44.2)	11 (24.4)
1	28 (59.6)	25 (52.1)	22 (51.2)	34 (75.6)
2	3 (6.4)	5 (10.4)	2 (4.7)	0 (0)
Type of myeloma, n (%)				
IgG	27 (57.4)	22 (45.8)	30 (69.8)	25 (55.6)
Non-IgG	7 (14.9)	12 (25.0)	5 (11.6)	5 (11.1)
Light chain	7 (14.9)	9 (18.8)	6 (14.0)	10 (22.2)
Unknown	6 (12.8)	5 (10.4)	2 (4.7)	5 (11.1)
R-ISS disease stage, n (%)				
I	10 (21.3)	12 (25.0)	6 (14.0)	10 (22.2)
II	27 (57.4)	23 (47.9)	27 (62.8)	26 (57.8)
III	7 (14.9)	12 (25.0)	7 (16.3)	8 (17.8)
Unknown	3 (6.4)	1 (2.1)	3 (7.0)	1 (2.2)
Cytogenetic risk, n (%)				
Standard risk	31 (66.0)	38 (79.2)	26 (60.5)	26 (57.8)
High risk ^a	12 (25.5)	7 (14.6)	11 (25.6)	14 (31.1)
Missing	4 (8.5)	3 (6.3)	6 (14.0)	5 (11.1)
Extramedullary disease by BICR, ^b n (%)				
Yes	20 (42.6)	19 (39.6)	20 (46.5)	15 (33.3)
No	27 (57.4)	29 (60.4)	23 (53.5)	30 (66.7)
Bone marrow plasma cells, n (%)				
< 50%	32 (68.1)	39 (81.3)	31 (72.1)	28 (62.2)
≥ 50%	13 (27.7)	4 (8.3)	7 (16.3)	13 (28.9)
Missing	2 (4.3)	5 (10.4)	5 (11.6)	4 (8.9)
Renal function, n (%)				
CrCl ≤ 60 mL/min	26 (55.3)	19 (39.6)	13 (30.2)	6 (13.3)
CrCl > 60 mL/min	21 (44.7)	29 (60.4)	30 (69.8)	39 (86.7)
Patients with ≥1 poor prognosis feature, ^c n (%)	36 (76.6)	30 (62.5)	29 (67.4)	31 (68.9)
No. of prior anticancer therapy line, median (range)	6 (2-22)	5 (2-13)	6 (3-12)	6 (2-14)
Patients who are triple-class exposed, ^d n (%)	47 (100)	48 (100)	43 (100)	45 (100)
Patients who are triple-class refractory, ^e n (%)	45 (95.7)	47 (97.9)	41 (95.3)	44 (97.8)
Patients who are penta-drug exposed, ^f n (%)	36 (76.6)	33 (68.8)	35 (81.4)	35 (77.8)
Patients who are penta-drug refractory, ^g n (%)	26 (55.3)	17 (35.4)	19 (44.2)	21 (46.7)
Refractory to last line of therapy, n (%)	46 (97.9)	46 (95.8)	38 (88.4)	40 (88.9)
Patients with prior BCMA-targeted therapy, n (%)	17 (36.2)	17 (35.4)	11 (25.6)	19 (42.2)
Median Baseline sBCMA (range), ng/mL	66.6 (1.31-511)	43.8 (3.87-467)	40.6 (3.96-606)	41.8 (0.274-575)

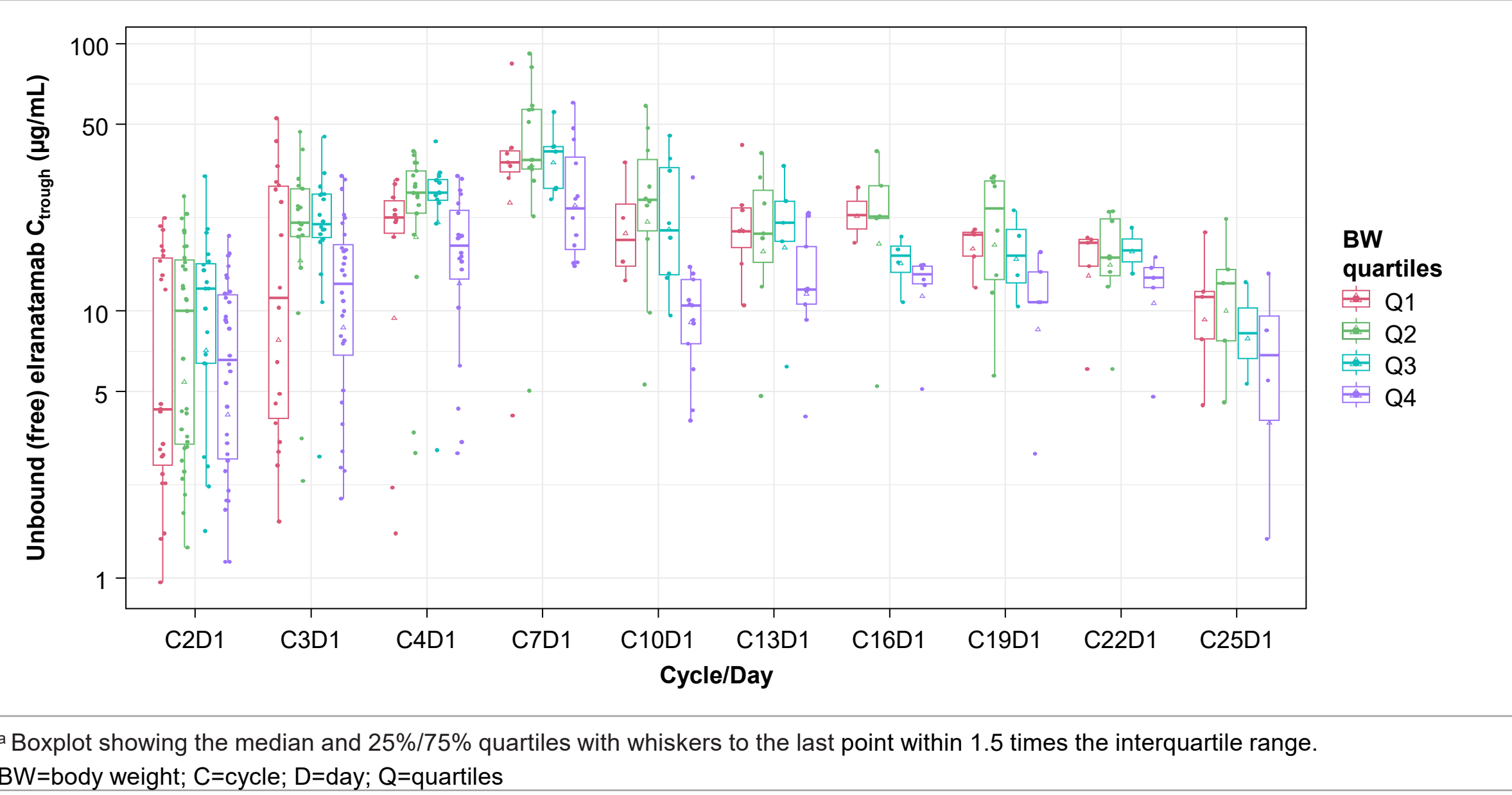
^a High risk if any of the following three chromosomal abnormalities of interest are present: T(4;14), T(14;16), DEL (17P). ^b Extramedullary disease was defined as presence of any plasmacytoma (extramedullary and/or paramedullary) with a soft-tissue component; ^c includes patients who have at least one of the following: ECOG performance status of 2, R-ISS of 3, EMD at baseline by BICR, high cytogenetic risk or bone marrow plasma cell involvement ≥50%; ^dReceived at least one PI, one IMiD, and one anti-CD38 mAb; ^eRefractory to at least one PI, one IMiD, and one anti-CD38 mAb; ^fReceived at least two PIs, two IMiDs, and one anti-CD38 mAb; ^gRefractory to at least two PIs, two IMiDs, and one anti-CD38 mAb.

BICR=blinded independent central review; BW=body weight; CrCl=creatinine clearance; ECOG=Eastern Cooperative Oncology Group; EMD=extramedullary disease; IgG=immunoglobulin G; IMiD=immunomodulatory drug; mAb=monoclonal antibody; PI=proleukin inhibitor; R-ISS=Revised Multiple Myeloma International Staging System; sBCMA=soluble B-cell maturation antigen

PK

- Elranatamab concentrations showed overlapping distributions with comparable medians across Q1 to Q3, with a lower median for Q4, which was not considered clinically relevant (**Figure 2**)

Figure 2. Elranatamab concentrations by BW quartile^a



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Methods

- Data from the phase 2 MagnetisMM-3 trial (NCT04649359) were used to evaluate the impact of BW on the PK, safety, and efficacy of elranatamab⁵
 - Patients were classified into quartiles (Q) according to their baseline BW to either Q1 (≤25th percentile), Q2 (>25th to ≤ median), Q3 (> median to ≤75th percentile), or Q4 (>75th percentile) (**Figure 1**)
 - This trial comprised 2 cohorts: Cohort A (n=123) included patients who had not previously received BCMA-directed therapy and Cohort B (n=64) included patients who had received prior BCMA-directed therapies
 - All patients received a 76-mg fixed dose of subcutaneous elranatamab after a 2-step priming dose regimen (12 mg on day 1; 32 mg on day 4)
- Blood samples were collected from MagnetisMM-3 trial patients for PK analysis

SAFETY

- There were no clinically relevant differences in the safety profiles across BW quartiles (n=183)
- Incidence of treatment-emergent adverse events (TEAEs) was 100% in all quartiles
- For BW quartiles Q1, Q2, Q3, and Q4, respectively:
 - Incidence of grade 3/4 TEAEs was 63.8%, 68.8%, 60.5%, and 84.4%
 - Incidence of serious TEAEs was 72.3%, 77.1%, 81.4%, and 71.1%
 - Discontinuations due to TEAEs occurred in 27.7%, 16.7%, 37.2%, and 28.9%

Table 2. TEAEs by BW quartile^a

Preferred term ^b	Any grade				Grade 3 or 4			
	Quartile 1 (n = 47)	Quartile 2 (n = 48)	Quartile 3 (n = 43)	Quartile 4 (n = 45)	Quartile 1 (n = 47)	Quartile 2 (n = 48)	Quartile 3 (n = 43)	Quartile 4 (n = 45)
Cytokine release syndrome	27 (57.4)	30 (62.5)	22 (51.2)	27 (60.0)	0 (0)	1 (2.1)	0 (0)	0 (0)
Anemia	25 (53.2)	27 (56.3)	27 (62.8)	20 (44.4)	19 (40.4)	23 (47.9)	21 (48.8)	15 (33.3)
Neutropenia	22 (46.8)	17 (35.4)	22 (51.2)	23 (51.1)	22 (46.8)	15 (31.3)	21 (48.8)	25 (51.1)
Thrombocytopenia	19 (40.4)	16 (33.3)	19 (44.2)	13 (28.9)	13 (27.7)	11 (22.9)	15 (34.9)	9 (20.0)
Hypokalemia	15 (31.9)	9 (18.8)	14 (32.6)	5 (11.1)	6 (12.8)	4 (8.3)	5 (11.6)	2 (4.4)
Pyrexia	15 (31.9)	16 (33.3)	10 (23.3)	12 (26.7)	1 (2.1)	1 (2.1)	2 (4.7)	2 (4.4)
Diarrhea	14 (29.8)	18 (37.5)	24 (55.8)	21 (46.7)	0 (0)	1 (2.1)	2 (4.7)	2 (4.4)
Asthenia	12 (25.5)	11 (22.9)	4 (9.3)	7 (15.6)	1 (2.1)	3 (6.3)	2 (4.7)	2 (4.4)
Lymphopenia	12 (25.5)	16 (33.3)	18 (41.9)	9 (20.0)	10 (21.3)	16 (33.3)	17 (39.5)	8 (17.8)
Decreased appetite	12 (25.5)	11 (22.9)	13 (30.2)	14 (31.1)	0 (0)	1 (2.1)	0 (0)	1 (2.2)
Cough	10 (21.3)	11 (22.9)	13 (30.2)	12 (26.7)	0 (0)	0 (0)	0 (0)	1 (2.2)
Nausea	9 (19.1)	11 (22.9)	9 (20.9)	11 (24.4)	0 (0)	0 (0)	0 (0)	0 (0)
Fatigue	9 (19.1)	14 (29.2)	17 (39.5)	13 (28.9)	0 (0)	1 (2.1)	2 (4.7)	1 (2.2)
Leukopenia	8 (17.0)	8 (16.7)	13 (30.2)	5 (11.1)	4 (8.5)	6 (12.5)	11 (25.6)	3 (6.7)
Headache	6 (12.8)	11 (22.9)	9 (20.9)	10 (22.2)	0 (0)	0 (0)	0 (0)	0 (0)
SARS-CoV-2 test positive	6 (12.8)	11 (22.9)	11 (25.6)	12 (26.7)	1 (2.1)	5 (10.4)	2 (4.7)	1 (2.2)

^a Data are presented as n (%) and are shown in descending order of proportion of patients with event in Quartile 1. Events presented if the reported occurrence was >20% of patients in the safety analysis set from any BW quartile.

^b The following clustered terms for cytopenias were used: thrombocytopenia (thrombocytopenia, platelet count decreased), anemia (anemia, hemoglobin decreased, red blood cell count decreased, hematocrit decreased, normochromic anemia, normocytic anemia, normochromic normocytic anemia), neutropenia (neutropenia, neutrophil count decreased, neutrophil percentage decreased, cyclic neutropenia, agranulocytosis, granulocytopenia, granulocyte count decreased), leukopenia (leukopenia, white blood cell count decreased), lymphopenia (lymphopenia, lymphocyte count decreased, lymphocyte percentage decreased, CD4 lymphocytes decreased, CD4 lymphocyte percentage decreased, CD8 lymphocytes decreased, CD8 lymphocyte percentage decreased).

BW=body weight; TEAEs=treatment-emergent adverse events

EFFICACY

- For Cohort A (n=123), overall response and complete response rates were comparable across BW quartiles (**Figure 3**)
- A clinically meaningful objective response rate benefit with overlapping confidence intervals was observed across quartiles, consistent with the primary efficacy analysis for Cohort A⁵ (**Figure 4**)
- No trend was identified between BW and progression-free survival (**Figure 5**) and the duration of response (**Figure 6**)

Figure 3. Responses by BICR by BW quartile (Cohort A)^a

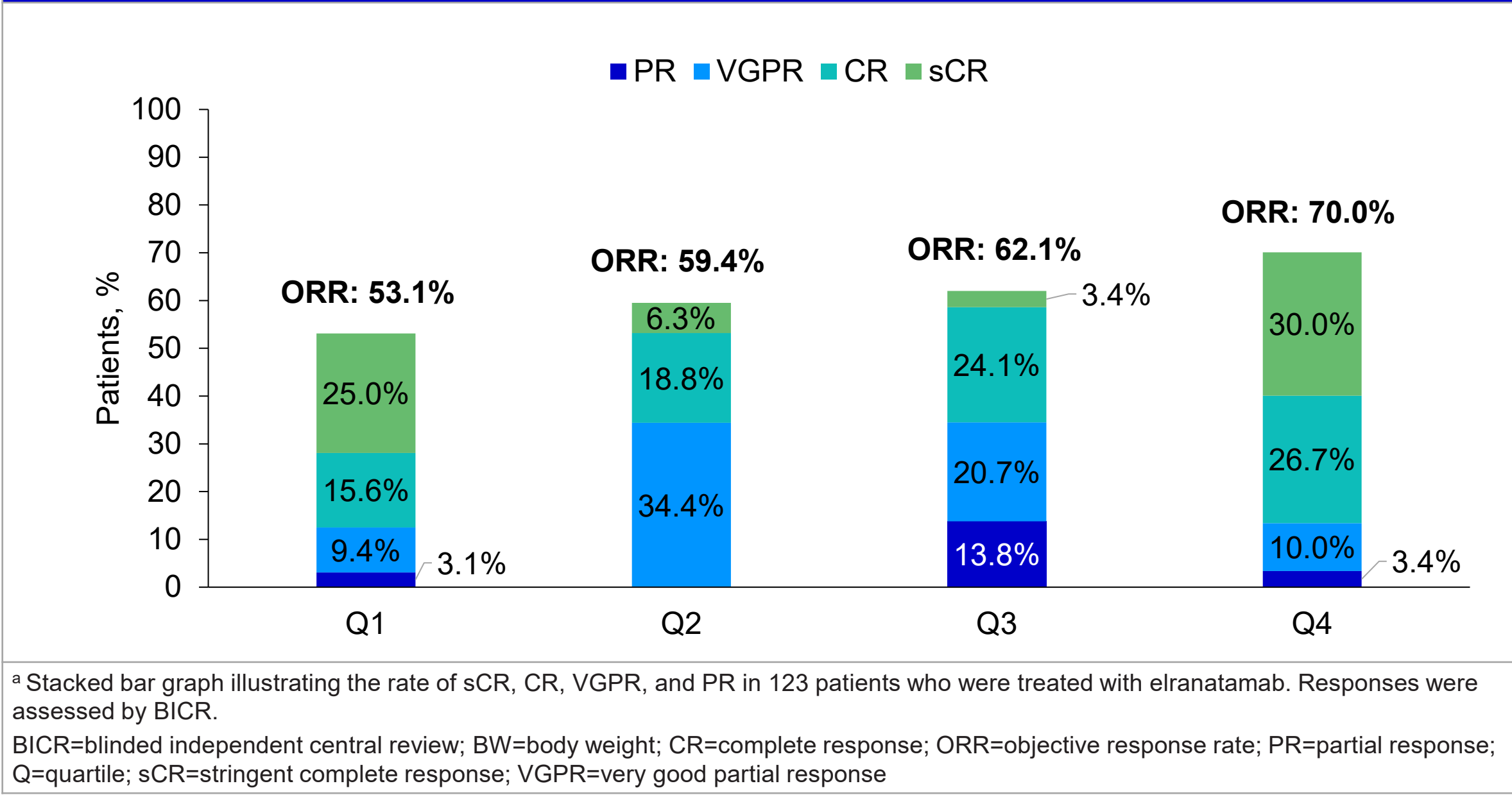


Figure 1. Overview of BW quartiles^a

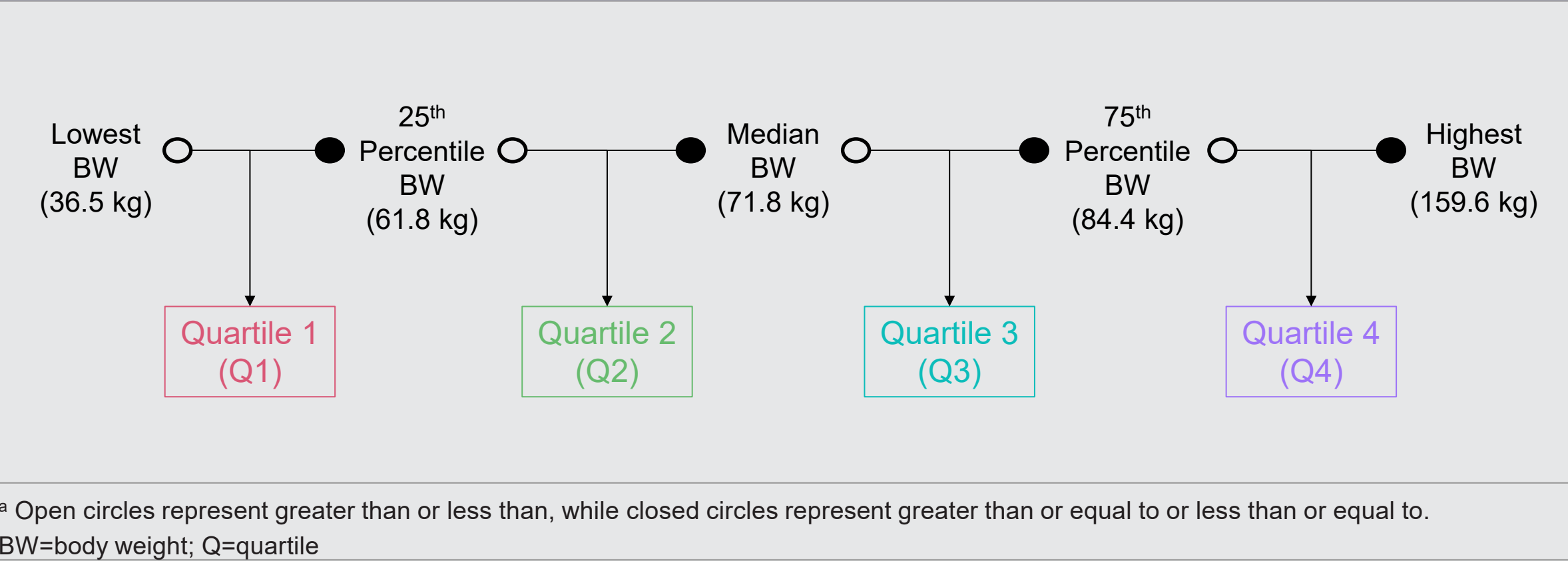


Figure 4. ORR by BICR by BW quartile (Cohort A)

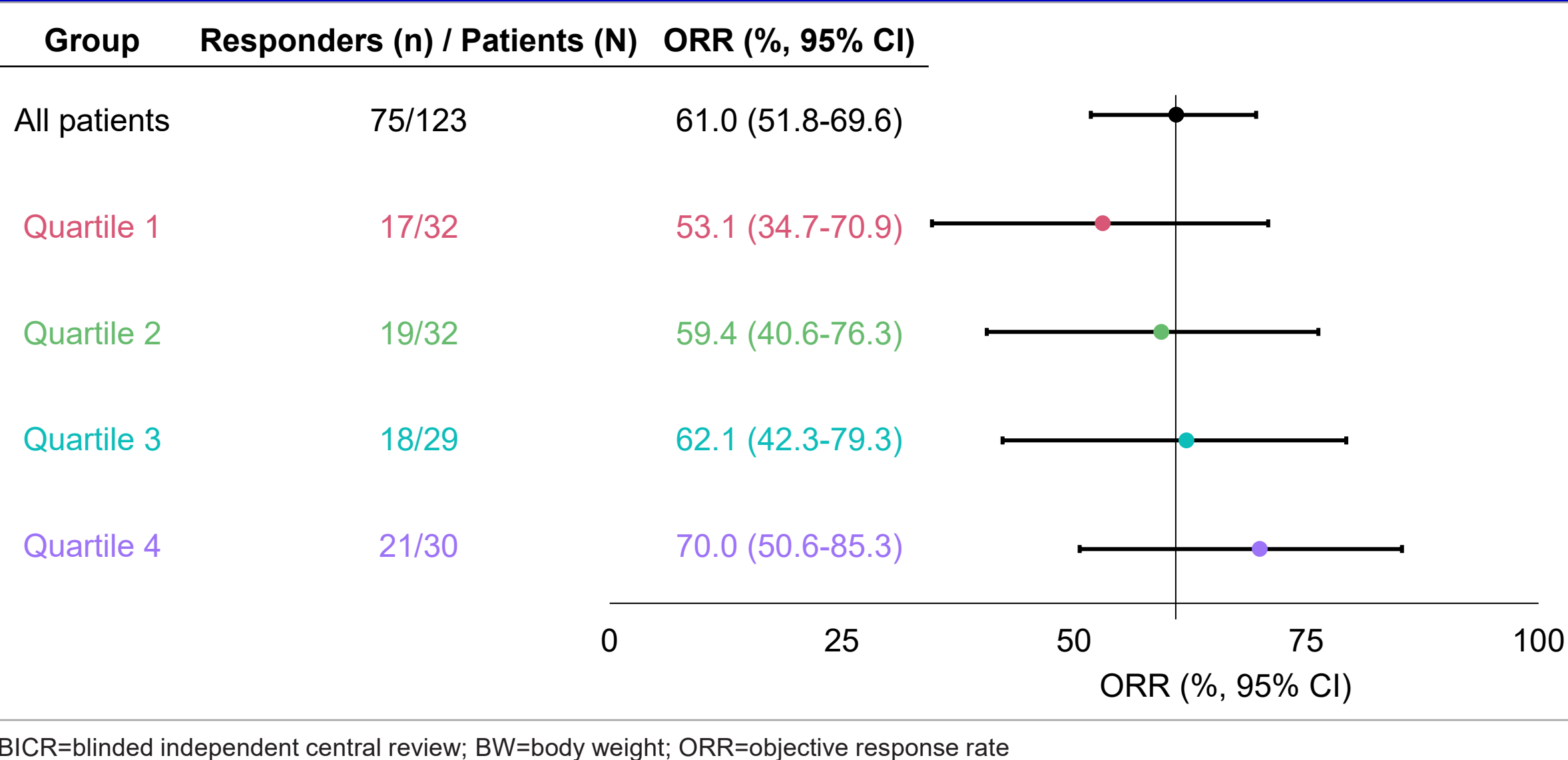


Figure 5. PFS by BICR by BW quartile (Cohort A)

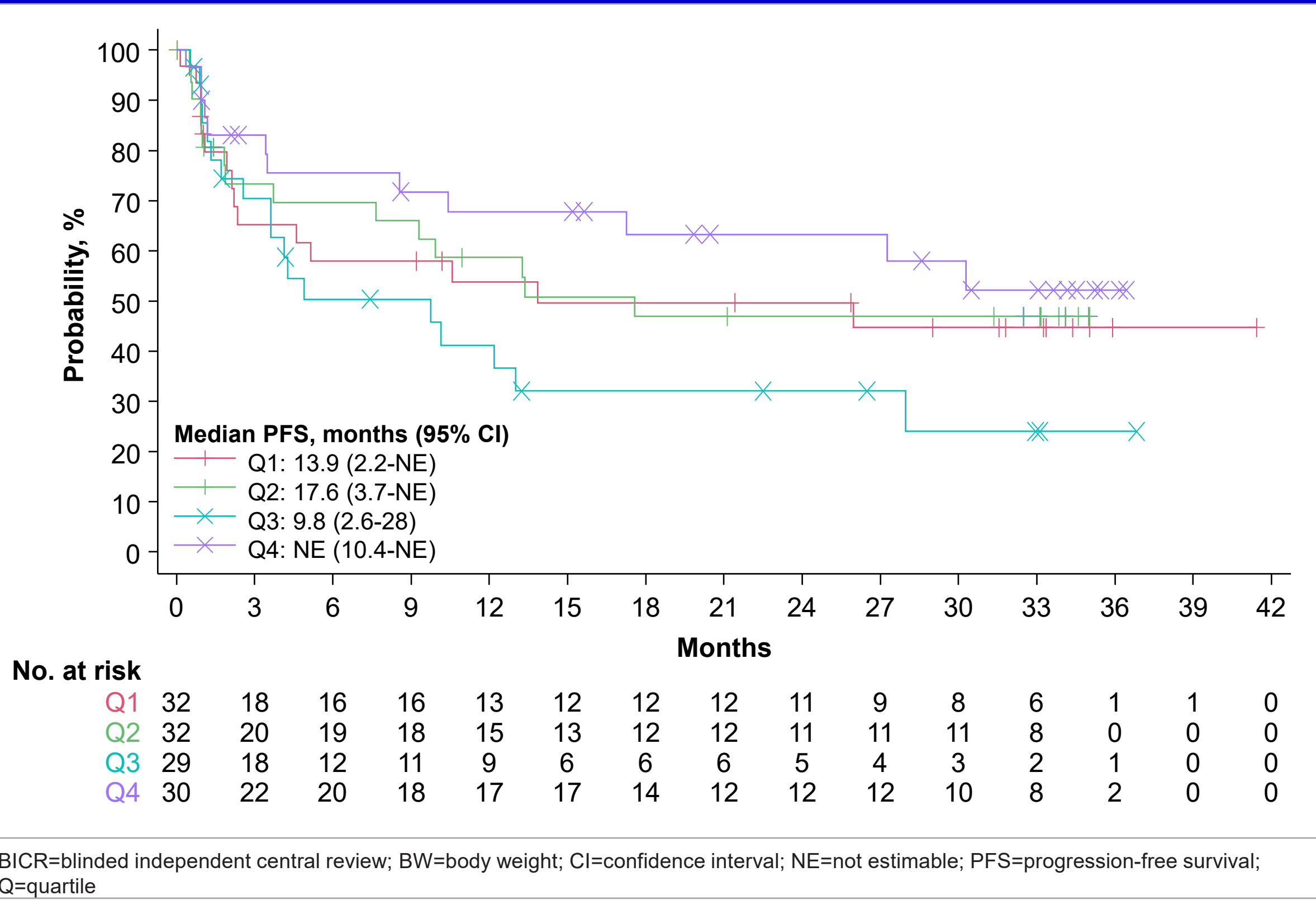


Figure 6. DOR by BICR by BW quartile (Cohort A)

