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Prior anti-BCMA antibody-drug conjugate exposure does not impact long-term outcomes with subsequent anti-BCMA T-cell-engaging bispecific antibodies: a single-center real-world data analysis

RUNNING TITLE: Impact of prior Belantamab on BCMA bispecific therapy

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AUTHORSHIP CONTRIBUTIONS

GB, ES and MFK designed the study and analyzed the data. GB, ES and MFK wrote the manuscript. All authors collected and curated data, revised and approved the manuscript.

CONFLICTS OF INTEREST

MFK: Abbvie: consultancy, honoraria; BMS: research funding; GSK: consultancy; Janssen: research funding, consultancy, honoraria; Karyopharm: consultancy; Pfizer: consultancy; Regeneron: consultancy; Takeda: consultancy.

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All other authors declare no conflict of interest.

DATA-SHARING STATEMENT.

De-identified data supporting the findings of this study are available from the corresponding author upon reasonable request and subject to applicable institutional and data protection regulations.

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B-cell maturation antigen (BCMA) has emerged as a key target for the treatment of patients with relapsed-refractory multiple myeloma (RRMM), with antibody-drug-conjugate (ADC) as well as for T-cell enganger (TCE) bispecific antibodies having been licensed by regulators and recommended for use by the UK National Health Service: the ADC belantamab-mafodotin (Belamaf) in second line as combination therapy(1); and TCEs elranatamab and teclistamab in fourth line and beyond(2,3). Myeloma patients treated in the NHS will therefore be exposed and refractory to anti-BCMA Belamaf, before being treated with anti-BCMA TCE. Questions about the efficacy of anti-BCMA TCE when sequenced after anti-BCMA ADC are therefore of high clinical relevance. Current evidence is inconclusive and focuses on response rates(4), but reports on long-term PFS effects are lacking. Recent reports suggest no significant BCMA antigen loss after ADC therapy(5), and the mechanism of action of Belamaf is different to TCE and not T-cell action dependent.
In addition, limited evidence has been published on the long-term PFS impact of high-risk cytogenetic abnormalities (HRCA) with TCE therapy; especially the cumulative quantitative prognostic effects of presence of 0, 1 or 2+HRCA(6).

To address these questions, we conducted an investigation into patients having completed at least 9 months of follow-up after start of TCE therapy at the Royal Marsden Hospital (RMH), London, UK.
An electronic health record (EHR) database search was conducted to identify RRMM patients who received standard of care (SOC) anti-BCMA TCE antibody (elranatamab or teclistamab) treatment at the Royal Marsden Hospital (RMH) NHS Foundation Trust between 1st July 2022 and 31st December 2024 and pseudonymised clinical information transferred into a secure database for analysis. Response was evaluated based on the modified International Myeloma Working Group (IMWG) response criteria(7). SOC cytogenetic information from the most recent bone marrow biopsy performed prior to TCE start was collected and included information on all HRCAs t(4;14), t(14;16), t(14;20), gain(1q), amp(1q), del(1p) and del(17p) for all patients.

Follow-up disease progression status and survival status were recorded with a data cut-off of 1st October 2025. Progression-free survival (PFS) was defined as the time from the date of start of TCE therapy to progression or death from any cause. Overall survival (OS) was defined as the time from the start of TCE to death from any cause. Cox regression analysis was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). All statistical analyses were undertaken using R version 4.3.3 and the ‘survival’, ‘survminer’ and ‘gtsummary’ packages. The study was reviewed and approved by the hospital’s Internal

Review Board (IRB) as a Service Evaluation (reference SE1445) and was conducted in accordance with the principles of the Declaration of Helsinki.

A total of 55 patients undergoing TCE therapy were identified and selected for analysis: 30 treated with teclistamab and 25 with elranatamab. Median age was 67 years (IQR 57–75), and clinical characteristics are summarized in **Table S1**. Fourteen patients (25%) had received Belamaf, and all were refractory to the ADC. Complete cytogenetic data were available for 52 patients. Radiological assessment at relapse (MRI or PET/CT) was performed in 50 patients: 10 (20%) had extramedullary disease and 12 (24%) had paraskeletal involvement. Of note, multiple patients would not have fulfilled common RRMM TCE trial criteria, due to pre-existing conditions including severe cardiac failure (n=1), psychiatric disorder (n=1), and history of cancer (n=2), previous BCMA exposure (n=14), non-secretory disease (n=7), severe cytopenia (n=1) or CNS involvement (n=1).

The median follow-up from treatment initiation was 19.7 months (IQR 17.2 - 30.76). For the overall cohort, median PFS was 9.8 months and did not differ significantly between teclistamab and elranatamab **(Figure S1, panel A and panel B)**. In this view, no statistically significant differences in clinical or genetic characteristics were observed between patients receiving teclistamab or elranatamab **(Table S1)**.

Patients received a median of 5 cycles of treatment (IQR 1-14). Overall response rate (ORR) was 73%; 15 patients (27%) were primary refractory to TCE. 31 patients (56%) achieved at least a very good partial response (≥VGPR), 19 (35%) achieved a complete response or better (≥CR).

Forty-one patients (74%) had discontinued TCE treatment by last follow-up. Treatment discontinuation was mainly due to disease progression (n=29), or toxicity (n=8). Other causes included patient decision (n=2) and occurrence of secondary primary malignancies requiring treatment (n=2). Of the 12 patients who discontinued TCE for reasons other than PD, 7 patients were still alive and in response at last follow-up. At the time of treatment discontinuation, the depth of response in these patients was PR in 1 patient, VGPR in 3 patients, and CR or better in 3 patients. Among them, one patient carries two HRCAs and 5 carry one HRCA. The median duration of treatment in these patients was 9.6 months (IQR 2.3–13.7), and the median time from treatment discontinuation to last follow-up was 11.6 months (IQR 4.2–16.3), with all patients maintaining their response throughout this period.

At the time of last follow-up, 25 patients had died. The majority of deaths (n=21) were due to disease progression, with the remainder due to infection (n=2) or second malignancy (n=2).

For the overall cohort, median OS was not reached **(Figure S2, panel A and panel B)**. Treatment duration, response, and survival outcomes are summarized in **Figure 1**.

Fourteen patients received prior Belamaf: 12 as monotherapy, 1 in combination with cyclophosphamide and dexamethasone (BCd), and 1 with bortezomib and dexamethasone (BVd). All 12 patients treated with single-agent Belamaf received this therapy immediately before switching to anti-BCMA TCEs.

The median time from the last dose of Belamaf to initiation of TCE therapy was 2 months (IQR 1–5). Twelve patients initiated Belamaf on a 3-weekly schedule, with less frequent dosing in the remaining 2 patients. Corneal toxicity led to Belamaf dose reductions in 2 patients, and dosing frequency reduction in 8 patients.

Four patients (28%) had been primary refractory to Belamaf, whilst 6 of 14 (42%) patients achieved ≥VGPR. All responder patients subsequently experienced disease progression on belantamab mafodotin and were therefore considered belantamab mafodotin-refractory prior to receiving.

ORR to TCE treatment for the 14 Belamaf-exposed and -refractory patients was 64% (1 partial response, 4 VGPR, 4 CR), three patients were primary refractory and 2 achieved stable disease (SD). Best responses of TCE-treated patients exposed to prior Belantamab are summarized in **Figure 2, panel A**. There was no obvious association between prior response to Belamaf and response to TCE. Long-term PFS with TCE did not differ significantly between Belamaf-exposed and -naive: 12 months PFS was 48% for Belamaf-exposed vs 53% for Belamaf-naive, and 24-month PFS 33% vs 38%, respectively (HR = 1.29; 95% CI 0.61–2.69; p = 0.5) **(Figure 2, panel B)**.

Of the 52 patients with available cytogenetic data, seven (14%) had 0 HRCA, 20 (37%) had 1 HRCA, and 25 (49%) had 2+ HRCAs. 12 months PFS was 71.4% for patients with 0 HRCA, 50% for 1 HRCA, and 36% for 2+ HRCAs. Compared to 0 HRCA, 1 HRCA had a PFS hazard ratio (HR) of 1.04 (95% CI 0.28–3.87; p = 0.96), and 2+ HRCAs a HR of 2.04 (95% CI 0.59–6.98; p = 0.26) **(Figure 3 panel A)**. Only one of the 0 HRCA patients was primary refractory to TCE. Two patients with 2 HRCA also experienced PFS of more than 24 months; both carried t(4;14) plus gain(1q). One of these patients had to stop TCE after two full doses of therapy due to side effects; the patient experienced VGPR which remained stable without further TCE therapy for 27 months and was ongoing at time of analysis.

Of other disease characteristics, extramedullary disease was associated with a markedly lower 12-months PFS of 20% (HR 3.25, 95% CI 1.33-7.91; p = 0.09), in keeping with previous reports. In this analysis, 12-months PFS was also lower with 41% months for those with paraskeletal plasmacytomas (HR 2.04, 95% CI 0.88–4.74; p = 0.09) **(Figure 3 panel B)**.

In this analysis, prior anti-BCMA ADC exposure did not adversely affect outcomes with subsequent anti-BCMA bispecific antibody therapy. This would be in keeping with emerging translational data on lack of BCMA loss after ADC, as well as with the T-cell independent effect of ADC. The sample size of our study is inherently limited and bias in patient treatment selection cannot be ruled out due to the non-randomized setting. However, multiple factors including the long-term follow-up and especially the reproducibility of well-established TCE risk factors such as extramedullary disease and high-risk cytogenetics, provide reassurance about the comparability of our cohort with a wider RRMM population. Nevertheless, the limited number of patients previously exposed to belantamab mafodotin does not allow definitive conclusions to be drawn regarding the optimal sequencing of anti-BCMA therapies. Rather, our findings should be considered hypothesis-generating and encouraging, warranting further validation in prospective clinical trials and larger real-world cohorts.

REFERENCES

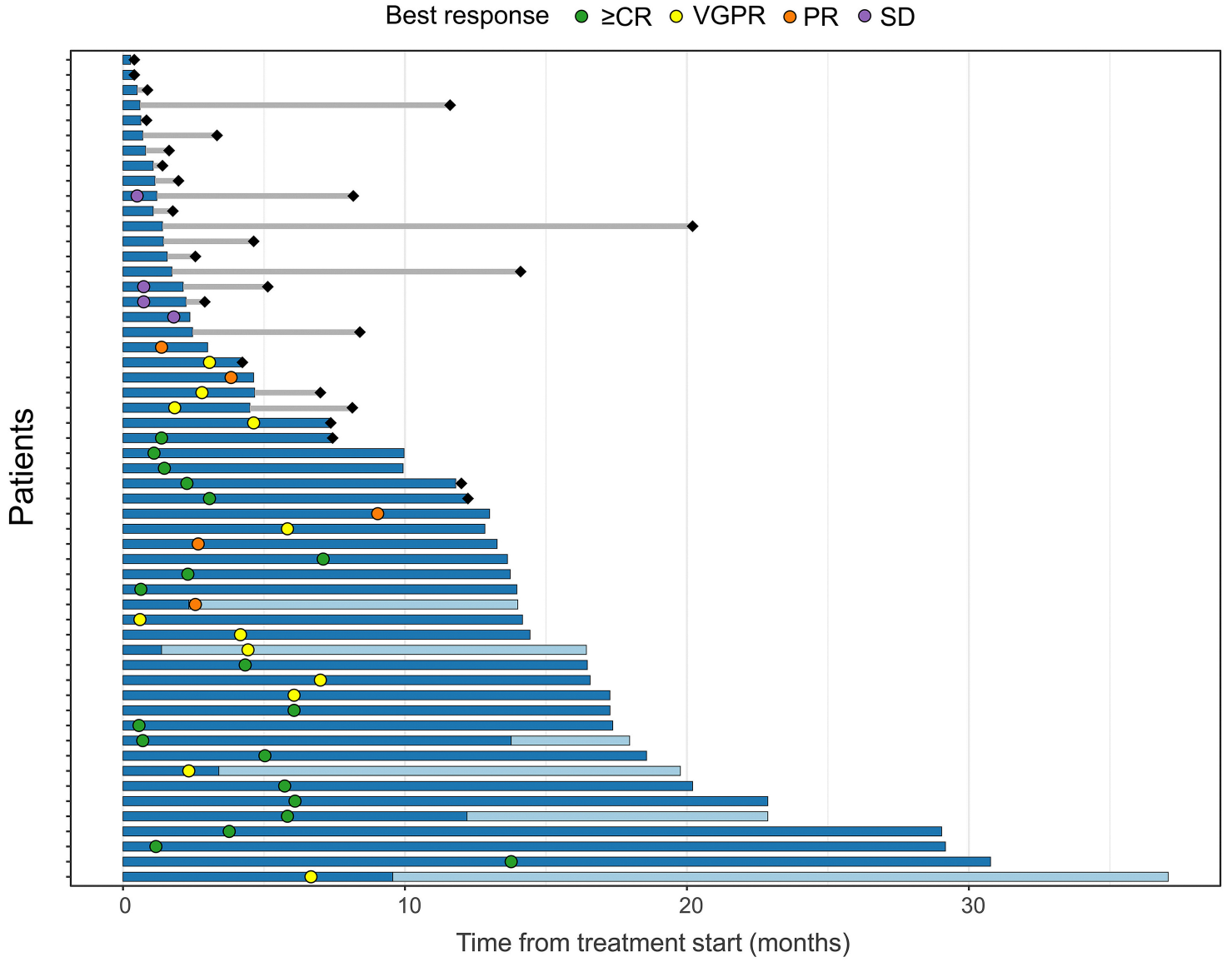
1. GlaxoSmithKline (GSK). Blenrep (belantamab mafodotin) combinations approved by UK MHRA in relapsed/refractory multiple myeloma. Available from: https://www.gsk.com/media/11946/press-release-blenrep-uk-mhra-approval_final.pdf. Accessed June 1, 2026.
2. National Institute for Health and Care Excellence (NICE). Teclistamab for treating relapsed and refractory multiple myeloma after 3 or more treatments. Available from: https://www.nice.org.uk/guidance/ta1015/chapter/1-Recommendations. Accessed June 1, 2026.
3. National Institute for Health and Care Excellence (NICE). Elranatamab for treating relapsed and refractory multiple myeloma after 3 or more treatments. Available from: https://www.nice.org.uk/guidance/ta1023/chapter/1-Recommendations. Accessed June 1, 2026.
4. Mewawalla P, Dileo R, Yin Y, et al. Real-world outcomes of sequential BCMA-directed therapies in relapsed refractory multiple myeloma after belantamab exposure. Clin Lymphoma Myeloma Leuk. 2025;25(12):e1007-e1013.
5. Musa H, Mielnik M, Trudel S, et al. Belantamab mafodotin does not induce B-cell maturation antigen loss or systemic immune dysfunction in multiple myeloma. Haematologica. 2026;11(2):665-678.
6. Kaiser MF, Sonneveld P, Cairns DA, et al. Co-occurrence of cytogenetic abnormalities and high-risk disease in newly diagnosed and relapsed/refractory multiple myeloma. J Clin Oncol. 2025;43(24):2679-2691.
7. Kumar S, Paiva B, Anderson KC, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. Lancet Oncol. 2016;17(8):e328-e346.

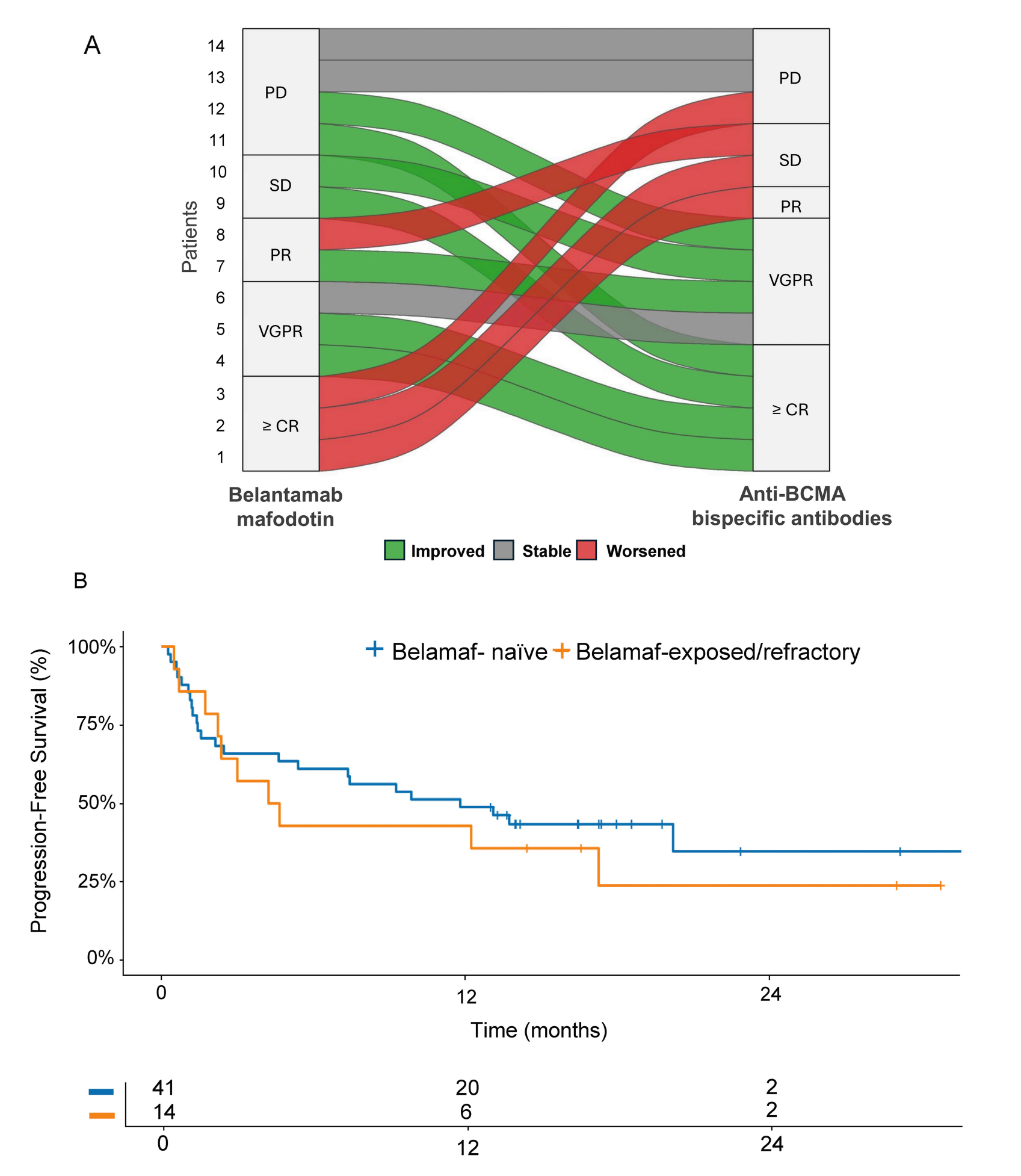
FIGURE LEGENDS

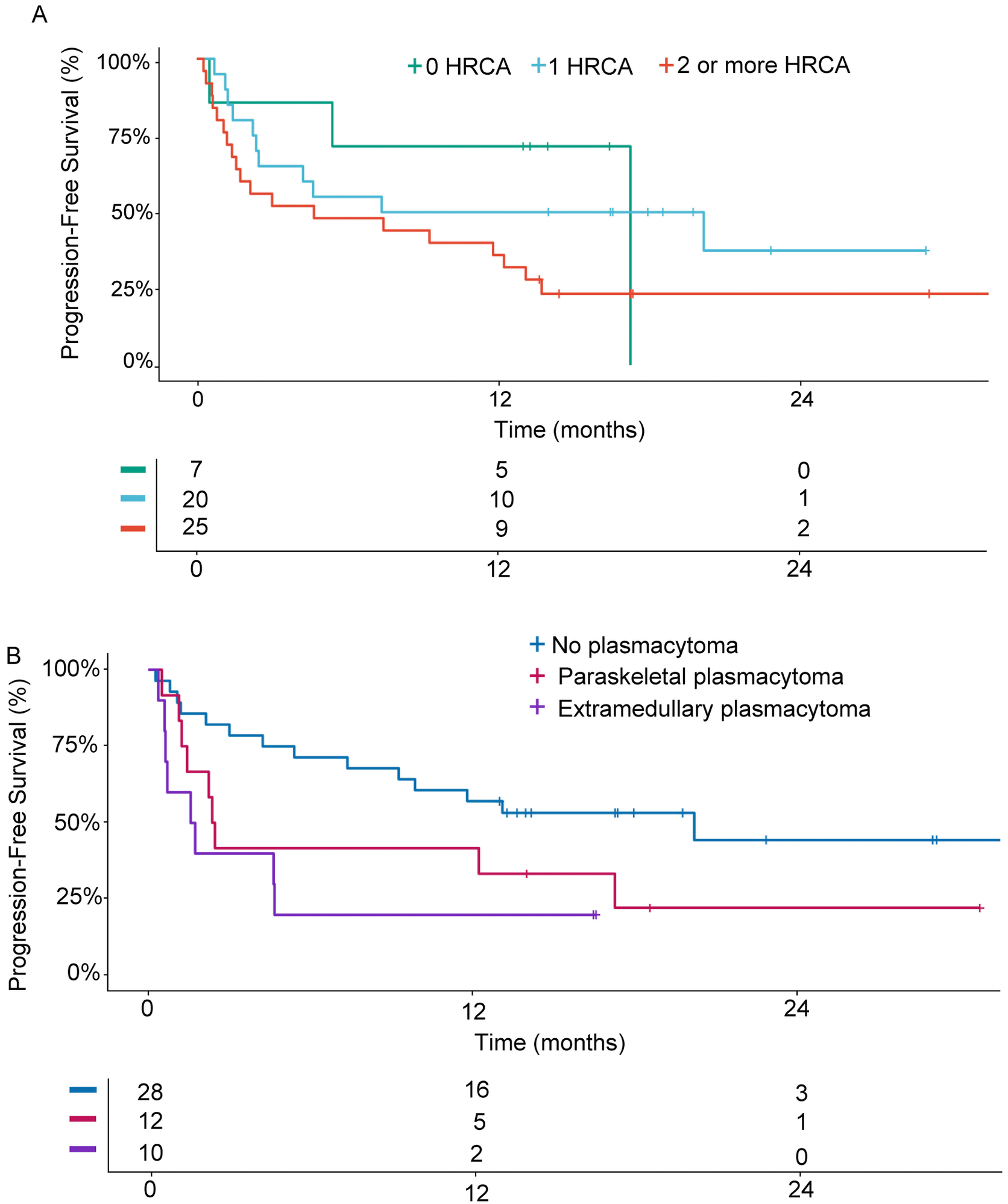
FIGURE 1. Swimmer plot summarizing treatment duration, response, and survival outcome. Blue bars indicate time on treatment from start to disease progression (PD). Circles indicate the best response: green ≥CR, yellow VGPR, orange PR, and purple SD. Light blue bars indicate time between treatment discontinuation and last follow-up without evidence of relapse. Grey lines indicate time from PD to death or last follow-up. Diamonds indicate death.

FIGURE 2. Outcomes in relation to previous treatment. Panel A shows best responses in TCE-treated patients previously exposed to belantamab; green bars indicate improvement in response, red indicate worsening, and grey indicate stable disease. **Panel B** shows progression-free survival (PFS) comparing belantamab-naïve versus belantamab-exposed/refractory patients.

FIGURE 3. Outcomes in relation to baseline characteristics. Panel A shows progression-free survival (PFS) according to the number of high-risk cytogenetic abnormalities (HRCAs): 0, 1, or ≥2. HRCAs are defined by the presence of t(4;14), t(14;16), t(14;20), 1q gain/amplification, del(1p), and del(17p). **Panel B** shows PFS according to plasmacytoma involvement (absence, paraskeletal, or extramedullary disease). This analysis includes only patients who had radiological assessments performed prior to treatment initiation.


Best response
≥CR
VGPR
PR
SD
Patients
0
10
20
30
Time from treatment start (months)


A
Patients
14
13
12
11
10
9
8
7
6
5
4
3
2
1
PD
SD
PR
VGPR
≥ CR
PD
SD
PR
VGPR
≥ CR
Belantamab mafodotin
Anti-BCMA bispecific antibodies
Improved
Stable
Worsened
B
Progression-Free Survival (%)
100%
75%
50%
25%
0%
Belamaf- naïve
Belamaf-exposed/refractory
0
12
24
Time (months)
41
14
20
6
2
2
0
12
24


A
Progression-Free Survival (%)
100%
75%
50%
25%
0%
0 HRCA
1 HRCA
2 or more HRCA
0
12
24
Time (months)
7
5
0
20
10
1
25
9
2
0
12
24
B
Progression-Free Survival (%)
100%
75%
50%
25%
0%
No plasmacytoma
Paraskeletal plasmacytoma
Extramedullary plasmacytoma
0
12
24
Time (months)
28
16
3
12
5
1
10
2
0
0
12
24

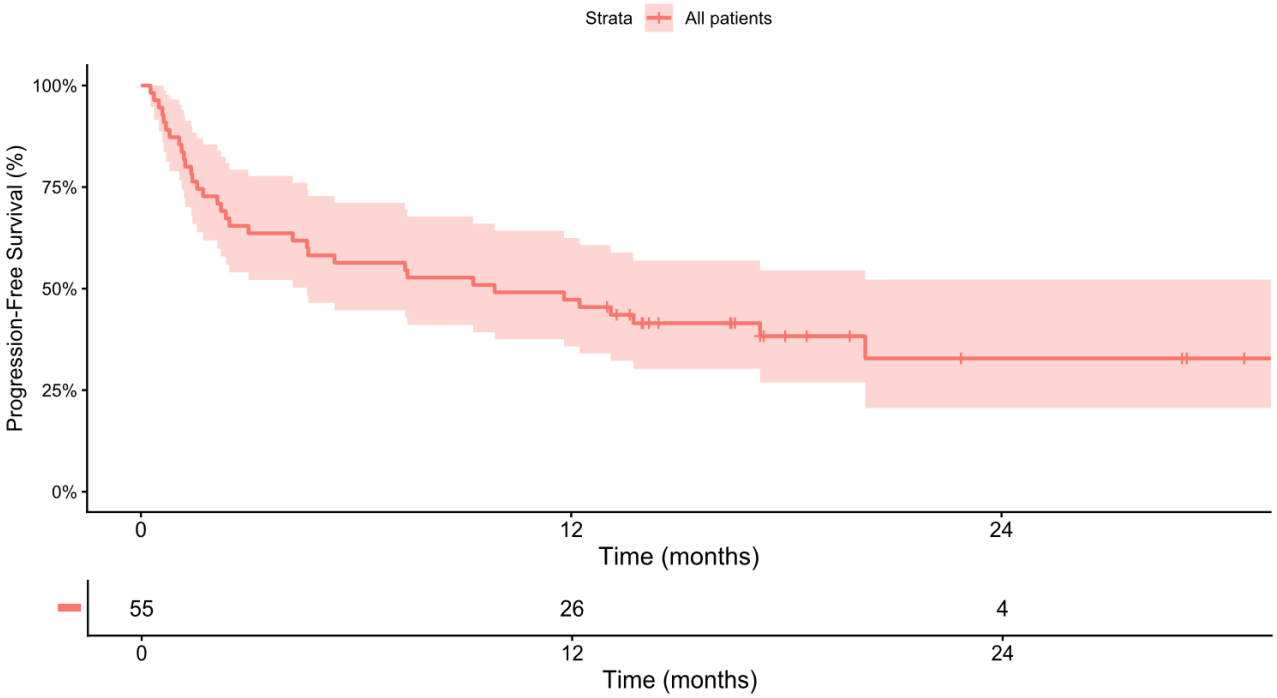
SUPPLEMENTARY MATERIAL

Table S1. Baseline patient characteristics and prior treatment details

Characteristic	**Overall N = 55**	**Elranatamab N = 30**	**Teclistamab N = 25**	**p-value**[1]
Age, Median (Q1, Q3)	67 (57, 75)	69 (57, 76)	66 (61, 73)	0.8
Sex, n (%)				0.10
Female	30 (55%)	13 (43%)	17 (68%)	
Male	25 (45%)	17 (57%)	8 (32%)	
Isotype, n (%)				
Light chain only	11 (20%)	7 (23%)	4 (16%)	0.6
M-protein	43 (78%)	22 (73%)	21 (84%)	
Non secretory	1 (2%)	1 (3%)	0 (0%)	
Cytogenetic data	52 (95%)	27 (90%)	25 (100%)	0.1
t(4;14) or t(14;16) or (t14;20) n (%)	15 (29%)	7 (26%)	8 (32%)	0.6
t(11;14), n (%)	4 (8%)	2 (7%)	2 (8%)	0.9
gain1q, n (%)	32 (62%)	19 (70%)	13 (52%)	0.2
amp1q, n (%)	6 (12%)	2 (7%)	4 (16%)	0.3
del1p, n (%)	13 (25%)	6 (22%)	7 (28%)	0.6
TP53 loss, n (%)	13 (25%)	4 (15%)	9 (36%)	0.08
Unknown	3	3	0	
HRCA, n (%)				0.3
0	7 (14%)	2 (7%)	5 (21%)	
1	20 (37%)	12 (44%)	8 (30%)	
2 or more	25 (49%)	13 (48%)	12 (50%)	
Unknown	3	3	0	
Plasmacytoma, n (%)				0.7
Extramedullary	10 (20%)	6 (21%)	4 (18%)	
Paraskeletal	12 (24%)	8 (29%)	4 (18%)	
Absence	28 (56%)	14 (50%)	14 (64%)	
*Unknown**	5	2	3	
Prior ASCT, n (%)	45 (82%)	25 (83%)	20 (80%)	0.9
Triple refractory, n (%)	48 (87%)	26 (87%)	22 (88%)	0.9
Penta refractory, n (%)	19 (35%)	8 (27%)	11 (44%)	0.3
Bela exposed, n (%)	14 (25%)	10 (33%)	4 (16%)	0.2

FIGURE S1.

Panel A. Progression-free survival of all patients included in the analysis.



Panel B. Progression-free survival stratified by bispecific antibodies.

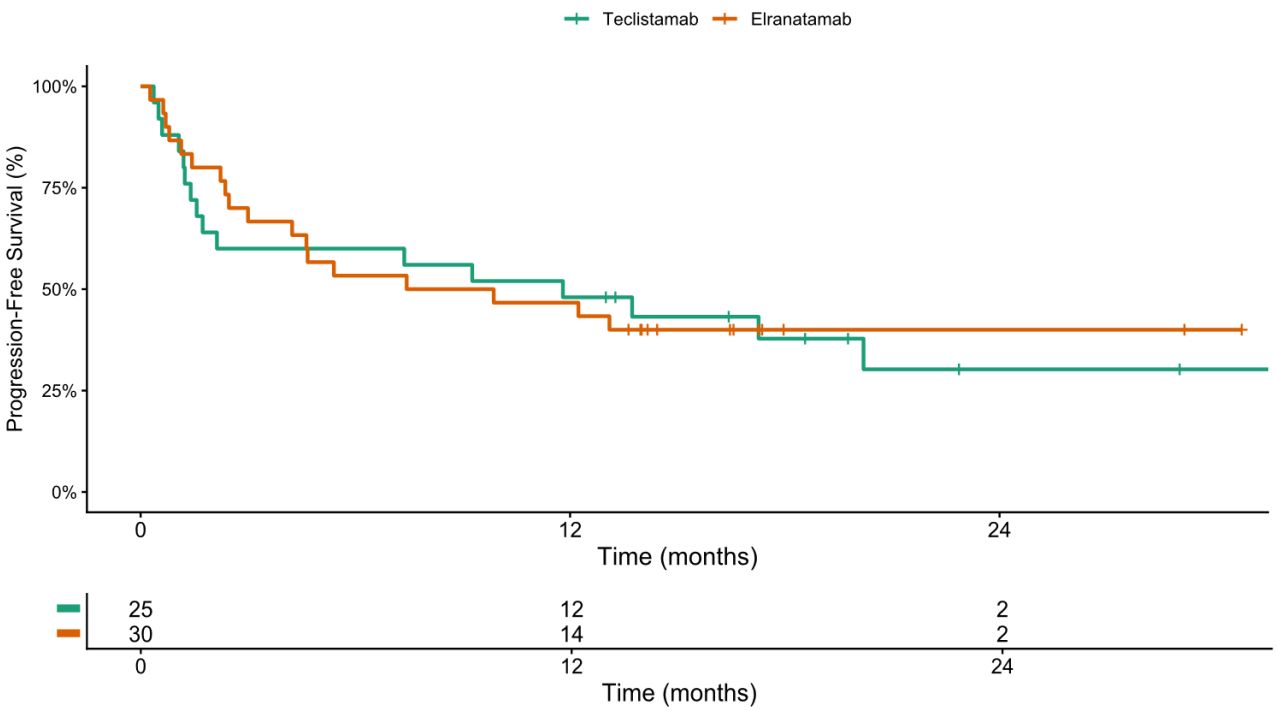
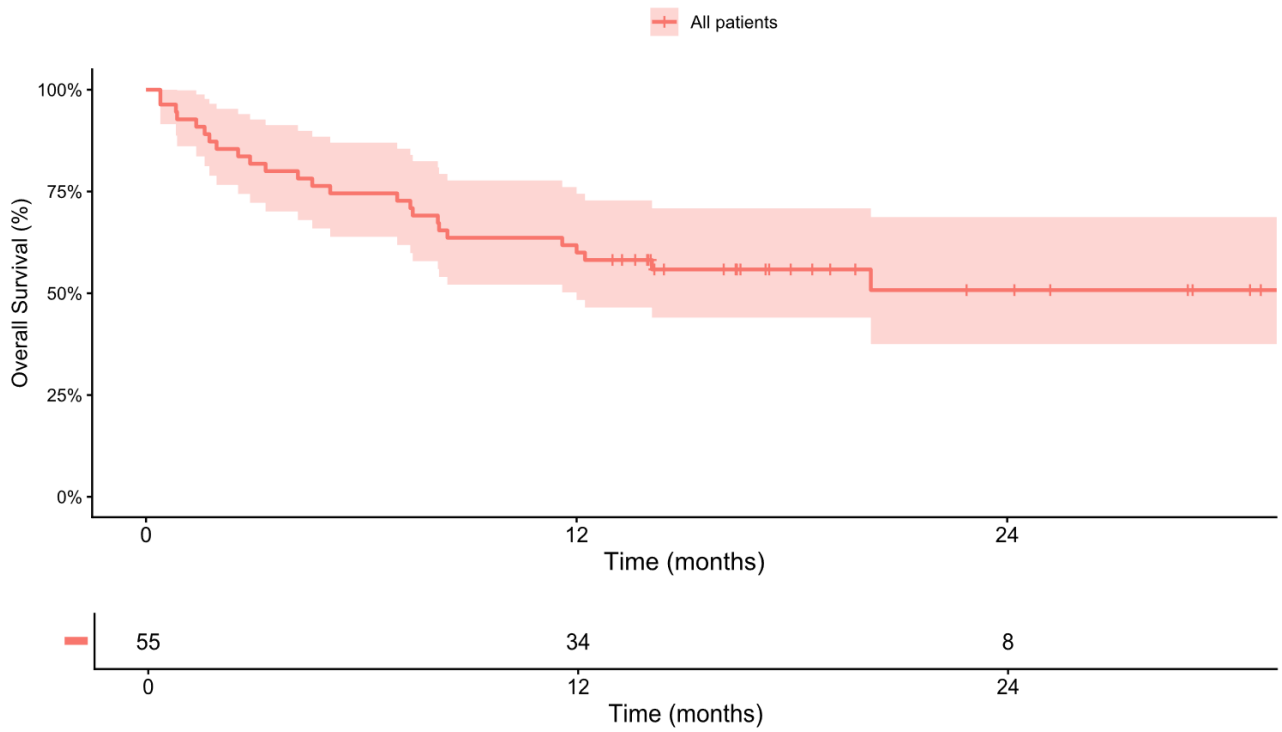


FIGURE S2.

Panel A. Overall survival of all patients included in the analysis.



Panel B. Overall survival stratified by bispecific antibodies.