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REAL-WORLD OUTCOMES OF GPRC5D- AND BCMA-TARGETING BISPECIFIC ANTIBODIES IN RELAPSED/REFRACTORY MULTIPLE MYELOMA: ACTIVITY FOLLOWING PRIOR BCMA EXPOSURE

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INTRODUCTION

As BCMA-directed therapies are increasingly incorporated earlier in the treatment algorithm of multiple myeloma, the post-BCMA therapeutic landscape is rapidly evolving. Treatment attrition across successive relapse lines significantly limits effective salvage options, particularly in frail patients underrepresented in clinical trials. Sequential antigen-targeted bispecific antibody (BsAb) therapy represents a biologically rational strategy to overcome antigen escape; however, real-world evidence remains limited.

We aimed to evaluate the real-world efficacy and safety of talquetamab (GPRC5D-targeting) and elranatamab (BCMA-targeting) in relapsed/refractory multiple myeloma (RRMM), with specific focus on outcomes according to prior BCMA exposure.

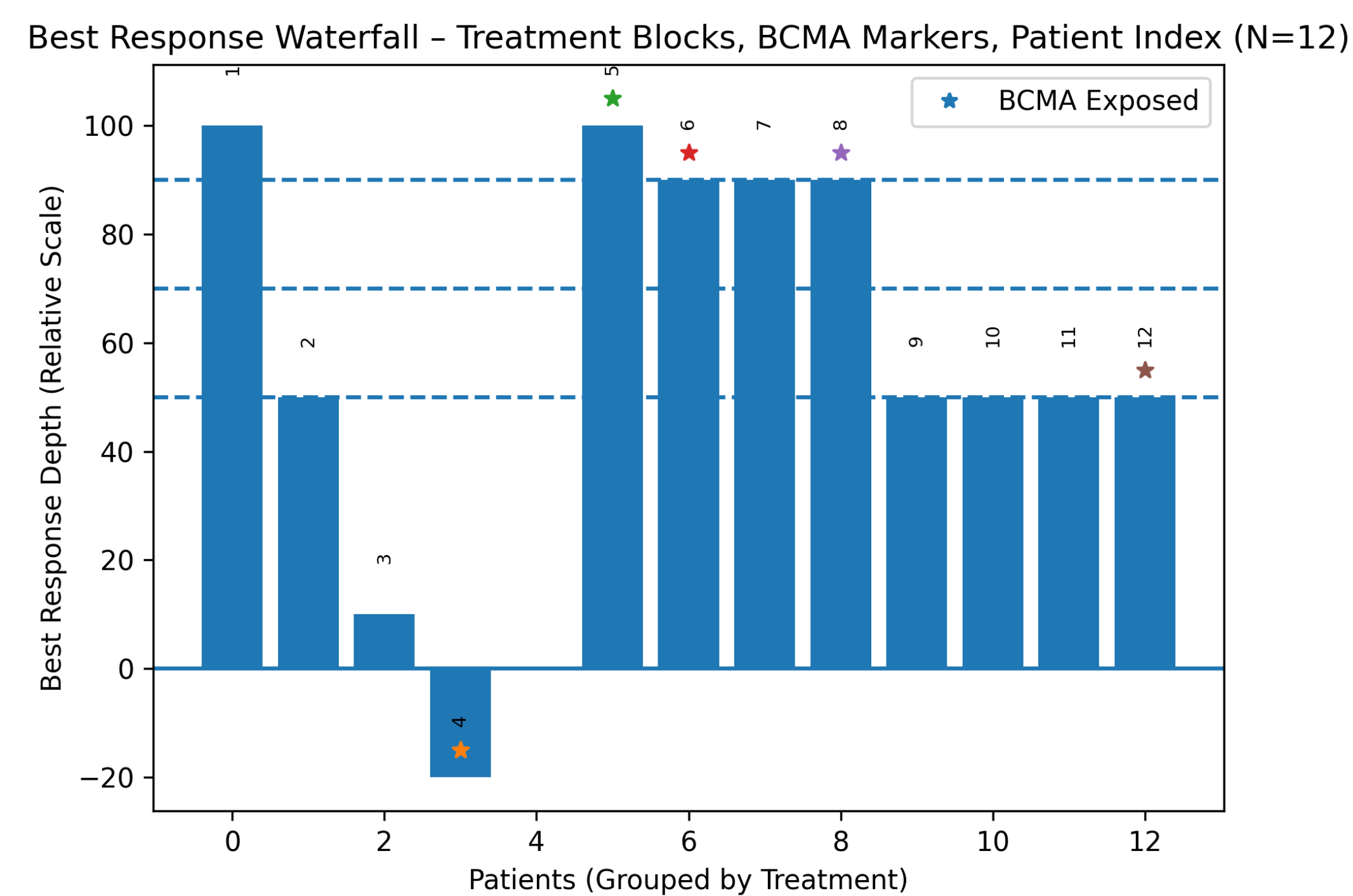
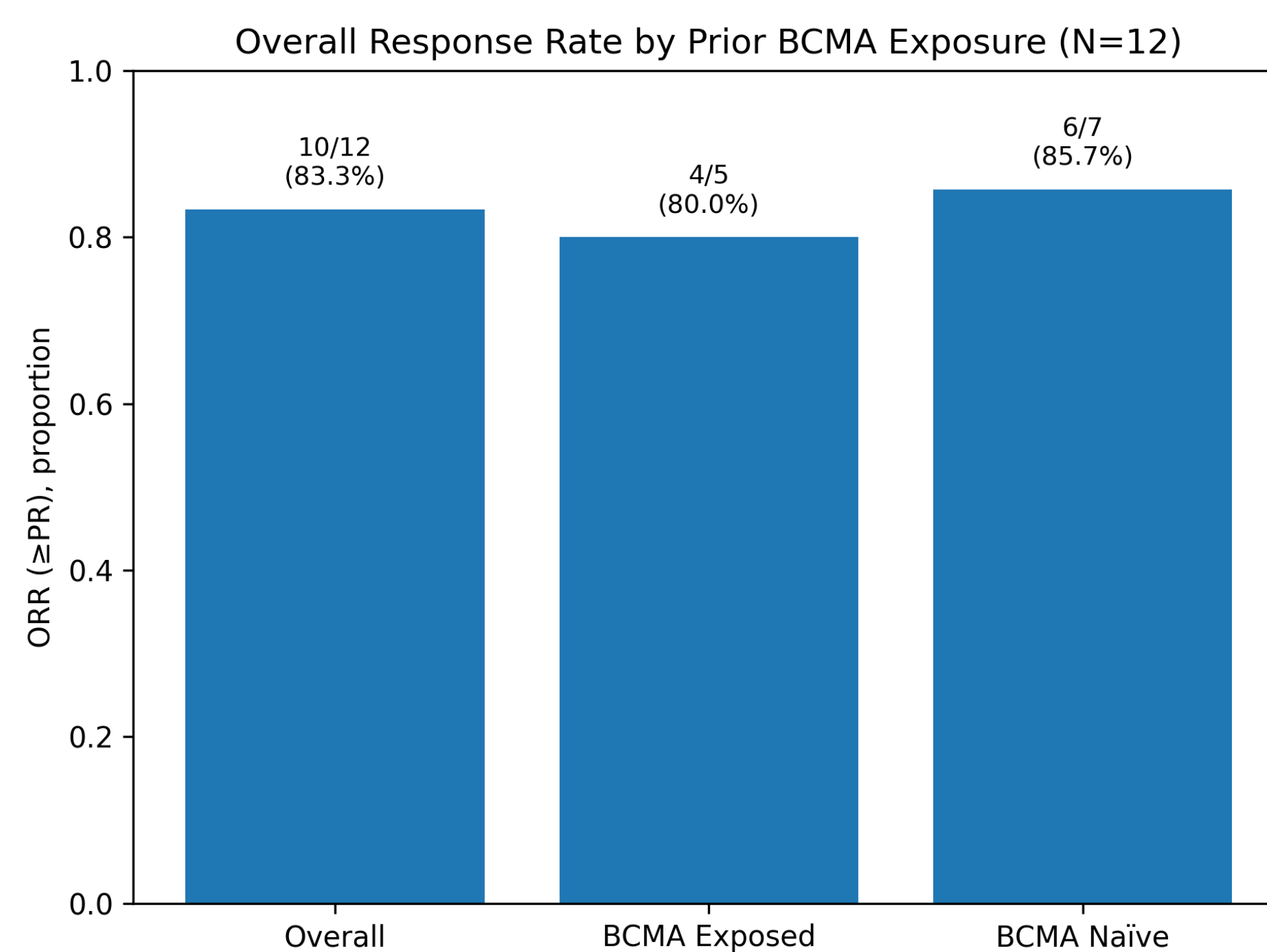
RESULTS

Twelve heavily pretreated RRMM patients were included, of whom five (41.7%) had prior BCMA exposure. The overall response rate (ORR) was 83.3% (10/12), with \geq VGPR achieved in 41.7% (5/12).

Clinical responses were observed irrespective of prior BCMA exposure (BCMA-exposed ORR 4/5; BCMA-naïve ORR 6/7), indicating preserved activity following BCMA-directed therapy. Talquetamab achieved an ORR of 8/8, while elranatamab achieved 2/4 responses.

Cytokine release syndrome (CRS) occurred in 5/12 patients, with grade \geq 2 events in one patient. ICANS and grade \geq 3 infection each occurred in one patient. Treatment discontinuation occurred in three patients.

Characteristic	N=12
Treatment	
Talquetamab	8 (66.7%)
Elranatamab	4 (33.3%)
Prior BCMA exposure	5 (41.7%)
ECOG \geq 2	6 (50%)
Efficacy	
ORR (\geq PR)	10/12 (83.3%)
\geq VGPR	5/12 (41.7%)
ORR – BCMA exposed	4/5 (80%)
ORR – BCMA naïve	6/7 (85.7%)
ORR – Talquetamab	8/8 (100%)
ORR – Elranatamab	2/4 (50%)
Safety	
CRS (any grade)	5 (41.7%)
\geq Grade 2 CRS	1 (8.3%)
ICANS	1 (8.3%)
\geq Grade 3 infection	1 (8.3%)
Discontinuation	3 (25%)



CONCLUSION

In this real-world RRMM cohort, bispecific antibody therapy demonstrated substantial clinical activity with manageable toxicity, including in patients previously exposed to BCMA-directed therapy. These findings support sequential antigen-targeted immunotherapy as a clinically relevant strategy and reinforce the emerging paradigm of immunotherapy layering rather than treatment class exhaustion in advanced disease.

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