NGS BASED ASSESSMENTS OF TREATMENT RESPONSE IN PATIENTS WITH MULTIPLE MYELOMA TREATED WITH BISPECIFIC T CELL ENGAGERS

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INTRODUCTION

- Bispecific antibodies (BsAbs) are currently approved for patients with relapsed/refractory multiple myeloma (RRMM), having demonstrated high rates of deep and durable responses in this population.
- Our study aims to evaluate the prognostic significance of FISH abnormalities, conventional karyotype, and laboratory parameters on PFS and OS in MM patients treated with BsAbs.

METHODS

- We performed a single-center retrospective analysis of 32 patients with BsAbs, including teclistamab, talquetamab, and elranatamab.
- Tempus xT next-generation sequencing (NGS) data were available for 28 patients (84.8%), obtained prior to or at BsAb initiation in 21 (75%) and on-treatment in 7 (25%).
- Pathogenic (PA), likely pathogenic (BR), and variants of uncertain significance (VUS) with VAF ≥10% were included; low confidence variants were excluded except in sensitivity analyses.
- Mutations were grouped into clinically relevant pathways.
- Kaplan-Meier estimation with log-rank testing assessed progression-free (PFS) and overall survival (OS). Fisher's exact test compared response rates.

CONCLUSIONS

- Our findings suggest that cytogenetic risk stratification retains prognostic relevance in the era of T-cell redirecting immunotherapy.
- Comprehensive cytogenetic and laboratory assessment may provide the most informative prognostic data for patients receiving BsAbs.

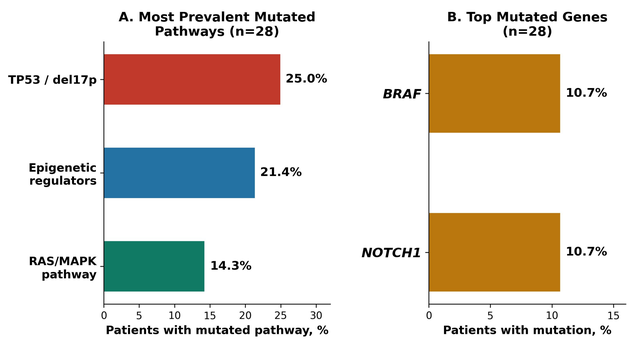
RESULTS

- Median age was 69 years (range 41–86); 48.5% were penta-refractory and 33.3% harbored high-risk cytogenetics.
- Overall response rate was 93.9%,with ≥VGPR in 81.8% and ≥CR in 36.4%.
- Among 28 patients with NGS data, the most prevalent mutated pathways were TP53/del17p (25%), epigenetic regulators (21.4%), and RAS/MAPK (14.3%).
- Top mutated genes included BRAF and NOTCH1 (10.7% each).
- TP53/del17p alterations (n=7) were associated with significantly inferior PFS (median 165 vs 734 days, p=0.015) and OS (median 264 vs 872 days, p=0.018) versus wild-type patients.
- No significant PFS, OS, or response differences were observed for RAS/MAPK or other pathways, likely reflecting limited statistical power.
- Penta-refractory status was associated with inferior PFS (median 183 vs 751 days, p<0.001) and OS (median 264 days vs not reached, p=0.001).
- Notably, no significant difference in PFS, OS, or response was observed between patients with PA/BR variants versus VUS-only variants across VAF thresholds using any VAF, or using only a VAF ≥ 10%, suggesting VUS mutations may contribute to disease biology and warrant further investigation.

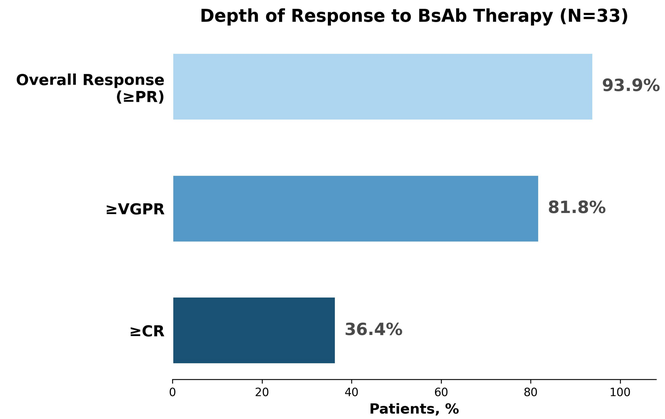
Baseline Cohort Characteristics

32	69 yrs	48.5%	33.3%	28 / 32
Patients treated with BsAbs	Median age (range 41–86)	Penta-refractory	High-risk cytogenetics	Patients with NGS data (84.8%)

Genomic Landscape of BsAb-Treated Patients with Available NGS Data (n=28/32, 84.8%)



Depth of Response to BsAb Therapy (N=33)



REFERENCES

Moreau P, Garfall AL, van de Donk NWCJ, Nahi H, San-Miguel JF, Oriol A, et al. Teclistamab in relapsed or refractory multiple myeloma. N Engl J Med. 2022;387(6):495-505.

Costa LJ, Bahlis NJ, Perrot A, Nooka AK, Lu J, Pawlyn C, et al. Teclistamab plus daratumumab in relapsed or refractory multiple myeloma. N Engl J Med. 2026;394(8):739-52.