

# GLP-1 RECEPTOR AGONIST EXPOSURE AND SURVIVAL OUTCOMES IN NEWLY DIAGNOSED MULTIPLE MYELOMA TREATED WITH DARATUMUMAB BASED QUADRUPLET THERAPY: A TARGET TRIAL EMULATION

COLTON JONES, MD <sup>1,2</sup>, TRAVIS STEUDBER, DO <sup>1</sup>, PARKER ROBERTS, MD<sup>1</sup>, MATTHEW BUTLER, MD<sup>1,2</sup>

- 1. University Of Texas Health Science Center At San Antonio, San Antonio, Texas
- 2. Mays Cancer Center, San Antonio, Texas



## INTRODUCTION

Obesity, insulin resistance, and chronic inflammation are associated with inferior outcomes in multiple myeloma (MM). Glucagon-like peptide-1 receptor agonists (GLP-1RAs) exert anti-inflammatory and immunomodulatory effects, including IL-6/NF-κB suppression and enhancement of cytotoxic immune cell function, that may synergize with anti-CD38-based immunotherapy. Retrospective data suggest GLP-1RA use is associated with reduced hematologic malignancy incidence and improved survival in patients with type 2 diabetes (T2DM), but no study has evaluated their impact specifically among patients receiving frontline daratumumab, bortezomib, lenalidomide, and dexamethasone (D-VRd).

## AIM

To evaluate whether concurrent GLP-1 receptor agonist use influences outcomes in patients with type 2 diabetes receiving frontline daratumumab, bortezomib, lenalidomide, and dexamethasone (D-VRd) for newly diagnosed multiple myeloma.

## METHOD

We emulated a target trial using the TriNetX Global Collaborative Network (>150 million patients, 112 healthcare organizations). Eligible patients were adults (≥18 years) with newly diagnosed MM, concurrent T2DM or obesity (BMI ≥30), initiating D-VRd. A landmark design at 90 days post-treatment initiation was employed to mitigate immortal time bias. The exposed cohort had documented GLP-1RA prescriptions spanning the landmark; controls were non-users. Propensity score matching (1:1) balanced age, sex, race, BMI, HbA1c, Charlson Comorbidity Index, ISS stage, and transplant receipt. The primary endpoint was overall survival (OS). Secondary endpoints included complete response (CR) or better and relapse. E-values were calculated to assess susceptibility to unmeasured confounding.

## CONCLUSIONS

GLP-1RA exposure was associated with a 70% reduction in mortality and higher deep response rates among patients with and without metabolic comorbidities receiving D-VRd. These findings suggest a potential metabolic-immune interaction in the quadruplet therapy era warranting prospective validation. Key limitations include residual confounding and observational response ascertainment.

## RESULTS

- After landmark application and matching, 1,042 patients were analyzed (n=521 per cohort).
- Cohorts were well balanced: median age 62 years; 59% White, 29% Black; 50% male; median BMI 32.
  - At median follow-up of 1,200 days, GLP-1RA exposure was associated with significantly improved OS (HR 0.30; 95% CI, 0.19–0.47; p<0.001; 25 vs. 70 deaths).
  - GLP-1RA users achieved higher rates of CR or better (HR 1.20; 95% CI, 1.03–1.49; p=0.02).
  - Relapse rates were not significantly different (HR 0.88; 95% CI, 0.68–1.14). The E-value for the OS estimate was 6.1.

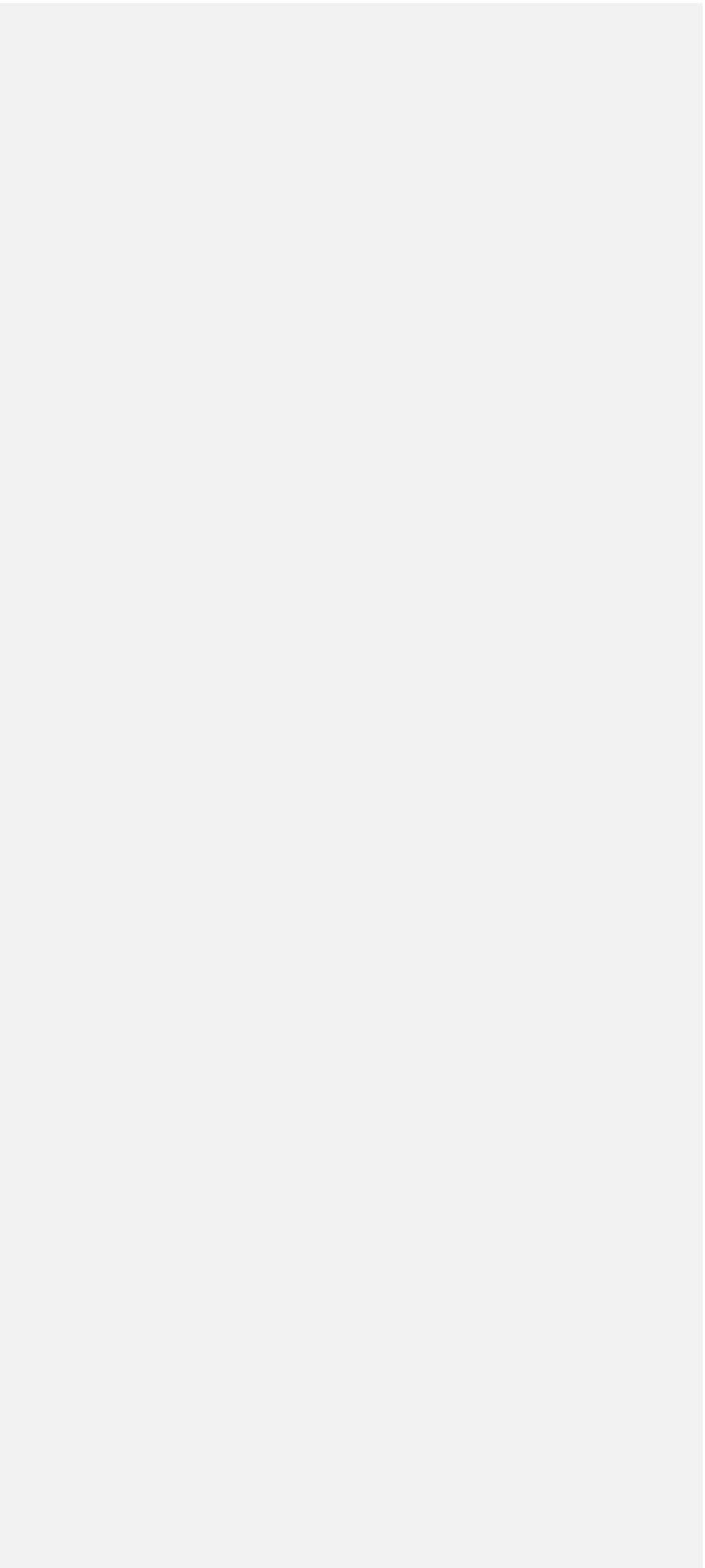
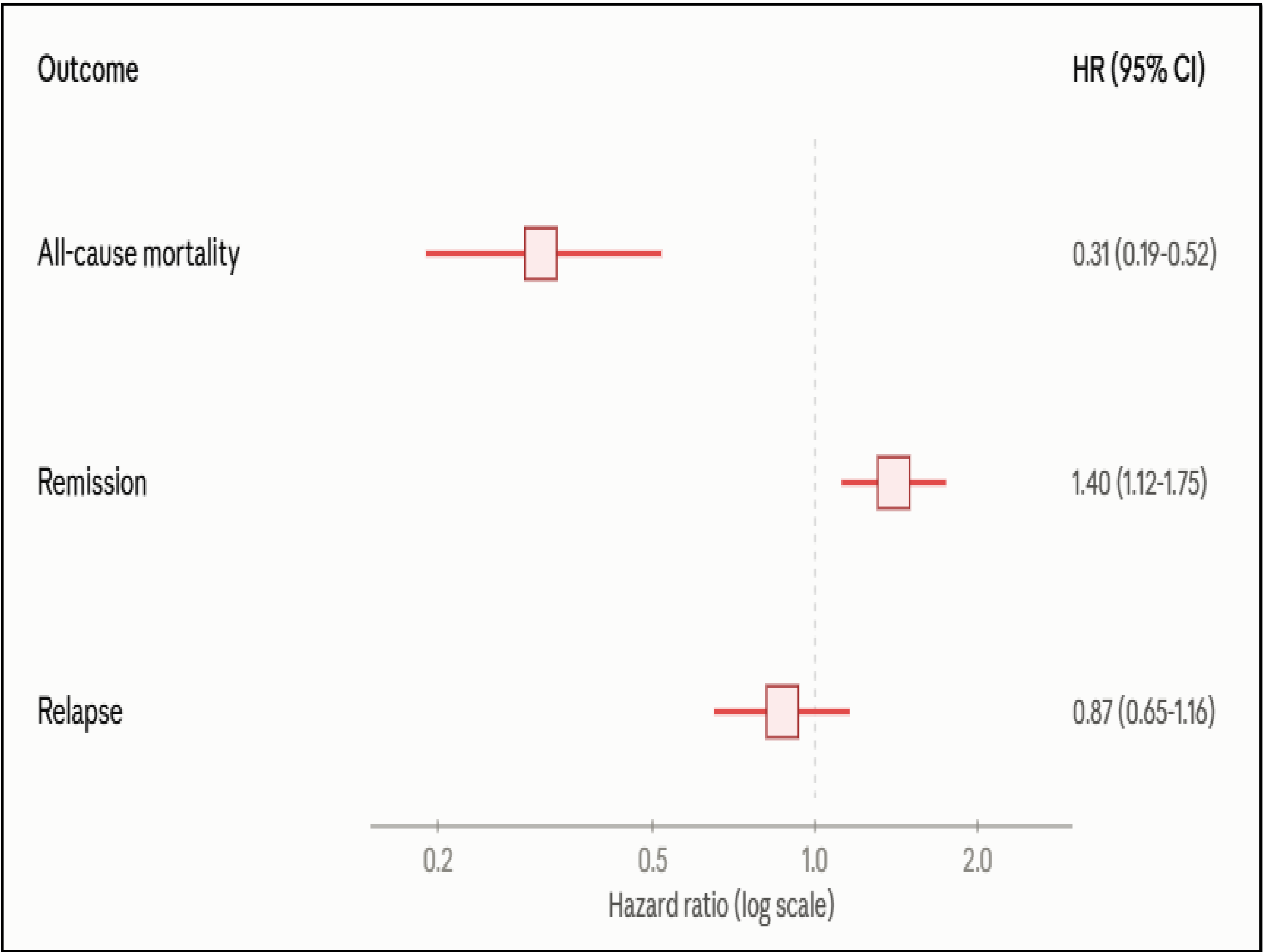


Figure 1: Hazard Ratios for All Cause Mortality, Relapse and Remission for the Treatment Cohort and Control Group



## ACKNOWLEDGEMENTS

We would like to dedicate this poster to our entire research team.

## CONTACT INFORMATION

Colton Jones, MD:  
Email: [jonesc17@uthscsa.edu](mailto:jonesc17@uthscsa.edu)  
X handle: theglpman

## REFERENCES

- 1.Obesity and Multiple Myeloma: Emerging Mechanisms and Perspectives. Seminars in Cancer Biology. 2023. Tentolouris A, Ntanasis-Stathopoulos I, Terpos E
- 2.A Comprehensive Review of the Impact of Obesity on Plasma Cell Disorders. Leukemia. 2022. Parikh R, Tariq SM, Marinac CR, Shah UA.
- 3.Adipokines, adiposity, and bone marrow adipocytes: Dangerous accomplices in multiple myeloma. Journal of Cellular Physiology. 2018. Morris EV, Edwards CM.
- 4.Impact of Body Mass Index on the Prognosis of Patients With Newly Diagnosed Multiple Myeloma. Blood Advances. 2025. Arnold KD, Ong KL, Ravi G, et al.
- 5.Body Mass Index and Multiple Myeloma: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies. BMC Cancer. 2026. Zahedi H, Eshaghian N, Hadizadeh M, Jowshan MR, Shadnough M