Acid Suppression and Plasma Cell Persistence: Does PPI Use Compromise the Efficacy of First-Line Daratumumab-Based Quadruplets?

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INTRODUCTION

Multiple myeloma (MM) treatment often involves daratumumab, bortezomib, lenalidomide, and dexamethasone (DVRd). While proton pump inhibitors (PPIs) are frequently co-prescribed to manage corticosteroid-induced dyspepsia, they can alter the gut microbiota and potentially interfere with the absorption or efficacy of oral therapies like lenalidomide. We evaluated the impact of concurrent PPI therapy on clinical outcomes in patients with newly diagnosed MM receiving DVRd.

AIM

To investigate if proton pump inhibitor use affects rates of remission, relapse, or overall survival in patients with multiple myeloma receiving daratumumab-based quadruplet therapy.

METHOD

Using the TriNetX Global Collaborative Network, we conducted a retrospective cohort study of adult patients with newly diagnosed MM across 112 healthcare organizations. Patients receiving DVRd without PPI (Cohort A) were propensity score-matched to those with ≥ 30 days of PPI exposure (Cohort B). The primary endpoint was overall survival (OS); secondary endpoints included relapse rates and minimal residual disease (MRD) negativity. We analyzed outcomes using Cox proportional hazards models.

CONCLUSIONS

Concurrent PPI use during DVRd therapy was associated with significantly higher rates of MRD negativity. However, DVRd without PPI demonstrated significantly lower relapse rates and a trend toward improved survival, despite lower rates of MRD negativity. The clinical benefit observed in the PPI group may stem from improved tolerance of dexamethasone-containing regimens, potentially leading to better treatment adherence. These findings suggest a complex relationship between acid suppression and MM outcomes, warranting further prospective investigation into the underlying mechanisms.

RESULTS

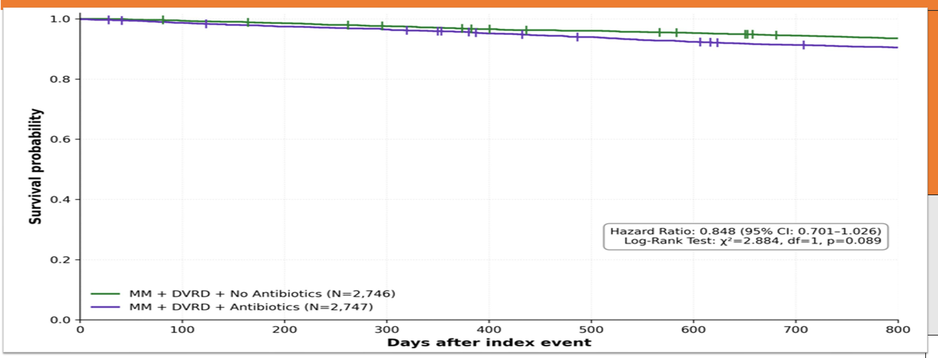

Figure 1: Kaplan-Meier Survival Curve

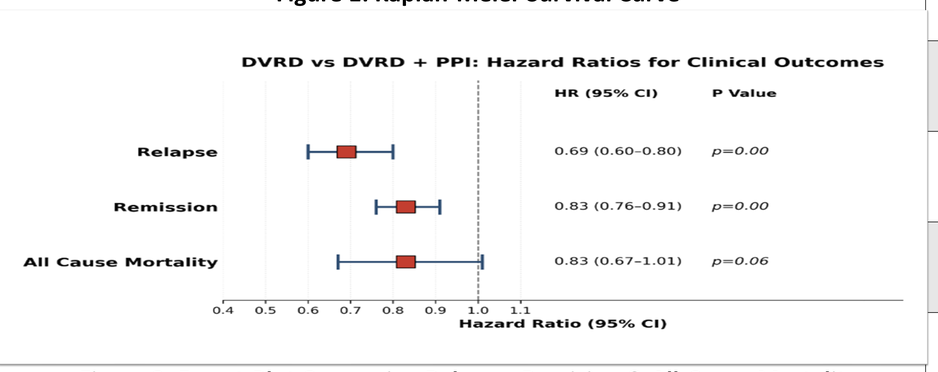

Figure 2: Forest-Plot Comparing Relapse, Remision & All-Cause Mortality

Characteristic	No PPI Group (n=2,265)	PPI Group (n=2,265)	Standard Mean Difference (SMD)
Age At Index Event	65.6 +/- 10.8 years	65.5 +/- 10.2 years	0.011
Female	999 (44.1%)	984 (43.4%)	0.012
Male	1,266 (55.9%)	1,281 (56.6%)	0.013
Black	445 (19.6%)	442 (19.5%)	0.003
White	1,503 (66.4%)	1,490 (65.8%)	0.012
Asian	81 (3.6%)	79 (3.5%)	0.005

CONTACT INFORMATION

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REFERENCES

1. Mahadevan A et al. GLP-1 receptor agonists in patients with cancer are associated with reduced all-cause mortality and hospitalization. J Clin Endocrinol. Metab 2026; May 19;111(6):1604-1612.

2. Ranc, K. *et al.* Mortality after cancer among patients with diabetes mellitus: effect of diabetes duration and treatment. *Diabetologia.* 2014; 57: 927–934.

3. Temperley HC, Kelly ME. Metabolic Modulation in Cancer Care: The Potential Role of Glucagon-Like Peptide-1 Receptor Agonists. J Clin Oncol. 2026 Jun 29: DOI: 10.1200/JCO-26-00062.

4. Ungvari Z, et al. Prognostic impact of glucagon-like peptide-1 receptor (GLP1R) expression on cancer survival and its implications for GLP-1R agonist therapy: an integrative analysis across multiple tumor types. Geroscience. 2025; 47(3):4413-4427. DOI: 10.1007/s11357-024-01494-5.

5. Wagle NS, et al. Cancer treatment and survivorship statistics, 2025. CA Cancer J Clin. 2025 Jul-Aug;75(4):308-340. doi: 10.3322/caac.70011.