Comparative Outcomes With Luspatercept Versus Erythropoiesis-Stimulating Agents in Lower-Risk Myelodysplastic Syndromes: A Propensity-Matched Retrospective Cohort Study

SOHO 2026 Annual Meeting | Poster # MDS-1271 | September 9-12, 2026 | Houston, TX

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INTRODUCTION

Lower-risk myelodysplastic syndromes (MDS) commonly cause chronic anemia and transfusion dependence. Erythropoiesis-stimulating agents (ESAs) have historically been used early, while luspatercept improves late-stage erythroid maturation. Direct real-world comparisons of longer-term clinical outcomes remain limited.

AIM

To compare survival and clinical outcomes with luspatercept versus epoetin alfa or darbepoetin alfa in adults with lower-risk MDS.

METHODS

Design: Retrospective active-comparator cohort study with propensity score matching.

Setting: TriNetX US Collaborative Network (67 participating HCOs in the attached analyses).

Population: Adults with lower-risk MDS; prior AML and stem-cell transplant were excluded.

Exposure: Mutually exclusive luspatercept and ESA cohorts; index therapy initiated after MDS diagnosis.

Matching: 1:1 PSM yielded 811 patients per group. Covariates included age, sex, race/ethnicity, CKD, hypertension, diabetes, hyperlipidemia, prior VTE, transfusion, chemotherapy, lenalidomide, hemoglobin, RDW, neutrophils, platelets, and iron.

Follow-up: Outcomes assessed from day 1 through 12 and 24 months after index therapy.

CONCLUSIONS

- Luspatercept was associated with lower all-cause mortality than ESAs at both 12 and 24 months.
- VTE, heart failure, and infection hospitalization were also lower at both time points.
- Transfusion, myocardial infarction, ischemic stroke, and transition to hypomethylating therapy were comparable.
- Residual confounding, treatment-selection bias, and coding-based outcome ascertainment limit causal inference; prospective validation is needed.

KEY RESULTS

Matched cohort: 811 patients per group

Outcome	12 mo: Lusp vs ESA	12-mo HR (95% CI)	24 mo: Lusp vs ESA	24-mo HR (95% CI)
Mortality	13.3% vs 22.2%	0.572 (0.450-0.726)	19.2% vs 29.1%	0.649 (0.530-0.794)
VTE	5.8% vs 9.5%	0.584 (0.406-0.839)	6.8% vs 10.5%	0.625 (0.445-0.878)
Heart failure	19.5% vs 24.7%	0.738 (0.599-0.909)	21.3% vs 26.9%	0.748 (0.613-0.914)
Infection hospitalization	15.9% vs 21.1%	0.711 (0.566-0.894)	20.0% vs 24.2%	0.796 (0.646-0.980)

Transfusion use and HMA transition were not significantly different at either time point.

CLINICAL INTERPRETATION

Associations favor luspatercept, but this observational analysis does not establish treatment causality.

ACKNOWLEDGMENTS

No external funding. Data were obtained from the TriNetX Research Network.

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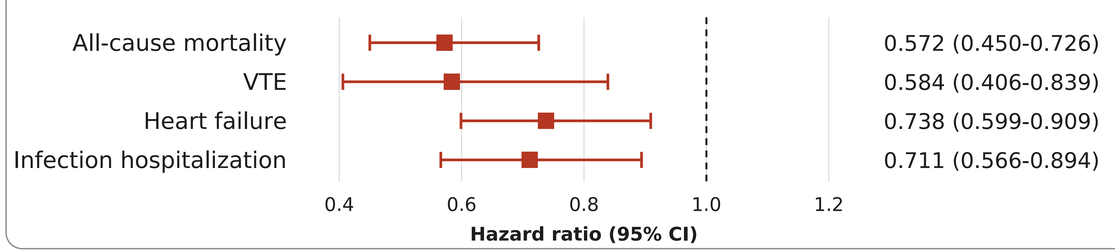
Adjusted associations at 12 months



Adjusted associations at 24 months