

Leukemic Transformation and Clinical Outcomes in Thrombocytopenic Myelodysplastic Syndrome Patients Treated with Thrombopoietin Receptor Agonists: A Real-World TriNetX Cohort Study

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BACKGROUND

Thrombopoietin receptor agonists (TPO-RAs) are used to manage thrombocytopenia in select patients with myelodysplastic syndromes (MDS), but concerns remain regarding the risk of leukemic transformation and thromboembolic events.

METHODS

- Conducted a retrospective propensity score-matched cohort study using data on adult patients with MDS from the TriNetX database.
- The exposed cohort had MDS treated with eltrombopag/romiplostim; the comparator cohort had MDS without exposure to either TPO-RA.
- Propensity score matching (N=4882) was performed for demographics, cardiovascular and thrombotic risk factors, thrombocytopenia, transfusion history, prior MDS-directed therapies, hematopoietic growth factors, and other baseline laboratory parameters.
- Kaplan-Meier survival analysis, hazard ratios (HRs) with 95% confidence intervals (CIs), and log-rank p-values were measured.

RESULTS

- AML transformation did not increase significantly in the TPO-RA cohort (HR 1.1, 95% CI 0.9–1.4, p=0.2), suggesting no statistically significant association between TPO-RA exposure and leukemic transformation within the first year.
- The risk of composite major bleeding, comprising gastrointestinal, mucosal/urinary, unspecified, and nontraumatic intracranial bleeding, was significantly higher at 1 year (HR 1.2, 95% CI 1.1–1.5, p=0.02) in the TPO-RA-treated MDS cohort.
- Anemia did not differ significantly at 1 year (HR 0.9, p=0.3). Neutropenia, used as a clinically relevant infection-risk surrogate for infection risk, was not significantly increased (HR 1.0, p=0.7) in the TPO-RA group.
- Stroke was significantly higher in the TPO-RA cohort at 1 year (HR 1.7, 95% CI 1.2–2.5, p<0.01). Pulmonary embolism was similarly increased (HR 2.3, 95% CI 1.4–3.7, p<0.01).
- All-cause mortality was significantly higher among patients treated with TPO-RA (HR 1.3, 95% CI 1.2–1.5, p<0.01).

CONCLUSION

- TPO-RA exposure was not associated with an increased risk of AML transformation at 1 year.
- TPO-RA-treated patients had higher all-cause mortality, thromboembolic events, and major bleeding. These findings may be limited by unknown residual confounding.
- Although the lack of an increase in short-term risk of leukemic transformation is reassuring, clinicians should thoroughly review comorbidities and prothrombotic states when considering TPO-RA for thrombocytopenia in MDS.

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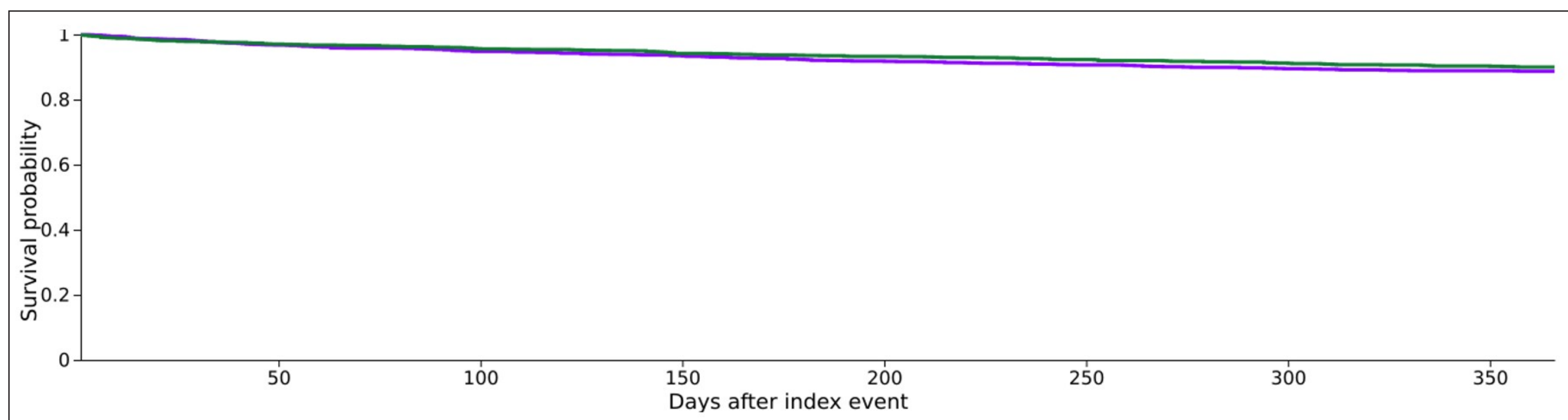


Figure 1: Kaplan-Meier survival curve comparing risk of AML transformation in patients with MDS with and without TPO-RA exposure

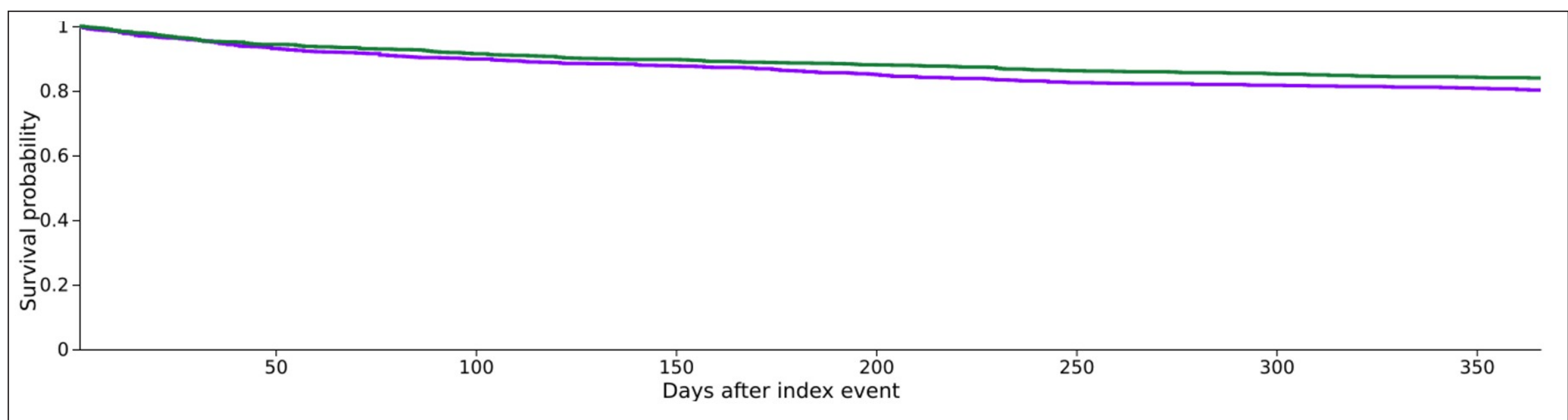


Figure 2: Kaplan-Meier survival curve comparing major bleeding in patients with MDS with and without TPO-RA exposure

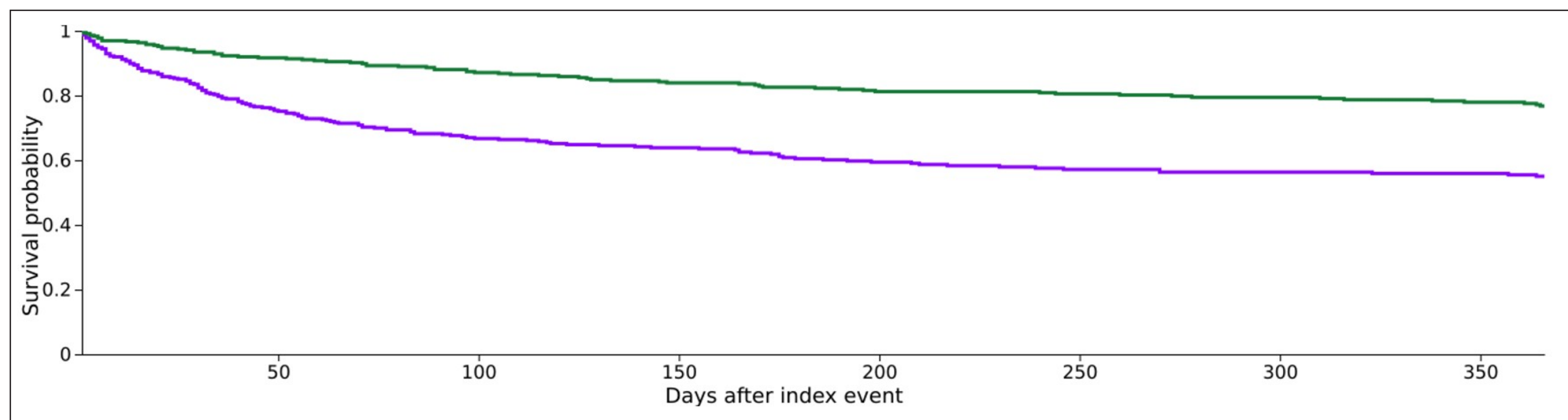


Figure 1: Kaplan-Meier survival curve comparing thrombocytopenia in patients with MDS with and without TPO-RA exposure

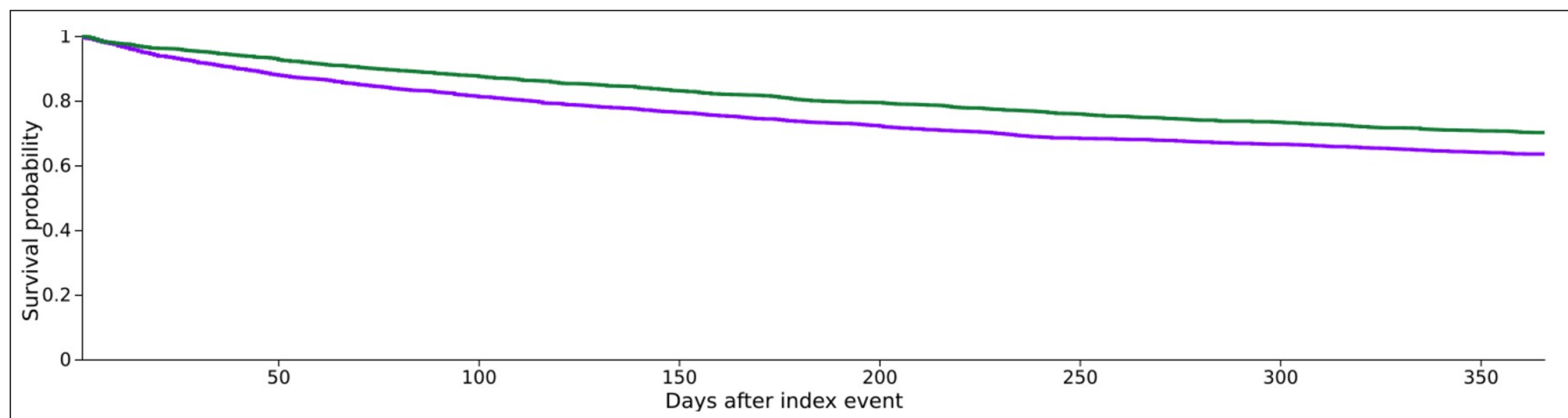


Figure 1: Kaplan-Meier survival curve comparing All-cause mortality in patients with MDS with and without TPO-RA exposure

— MDS patients with TPO-RA exposure
— MDS patients without TPO-RA exposure