Long-Term Risk of Clonal Evolution and Infectious Outcomes With Eltrombopag Plus Immunosuppressive Therapy in Idiopathic Aplastic Anemia: A Propensity-Matched Real-World Analysis

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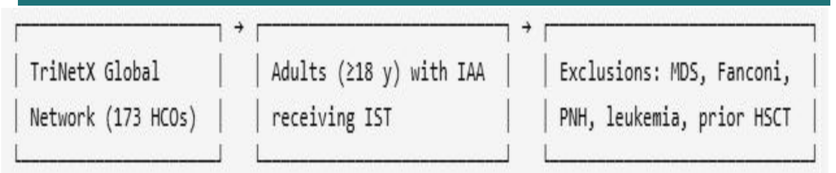
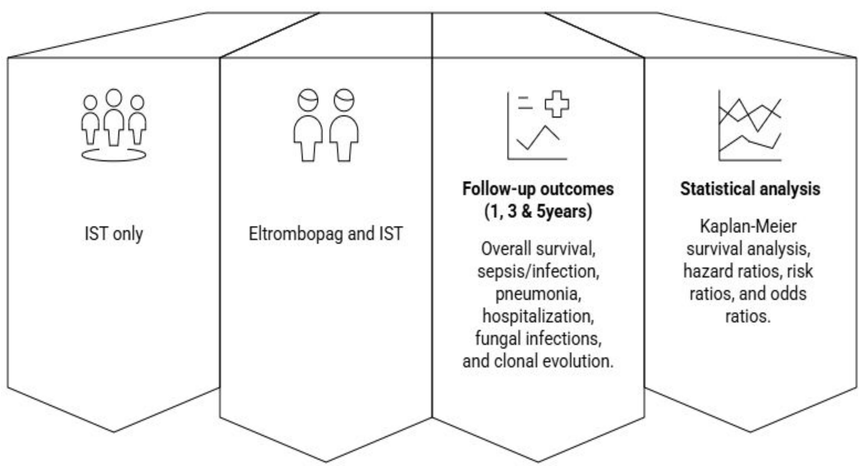
Background

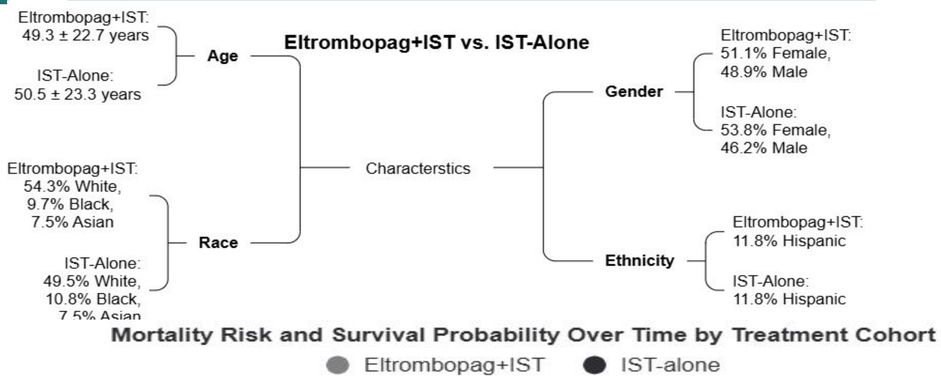
Idiopathic aplastic anemia (IAA) is a rare immune-mediated bone marrow failure disorder commonly treated with immunosuppressive therapy (IST), including antithymocyte globulin (ATG) and cyclosporine. Eltrombopag, a thrombopoietin receptor agonist, has demonstrated improved hematologic response rates in severe aplastic anemia; however, concerns remain regarding long-term clonal evolution to acute myeloid leukemia (AML) or myelodysplastic syndromes (MDS), as well as infectious complications in immunocompromised patients. This study evaluated the long-term risk of clonal evolution, survival, sepsis-related outcomes, pneumonia, hospitalization, and invasive fungal infections among patients with IAA treated with eltrombopag plus IST compared with IST alone.

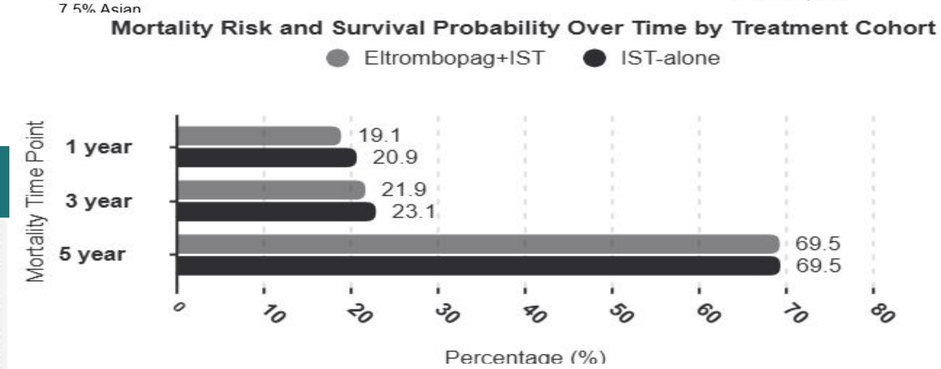
Methods

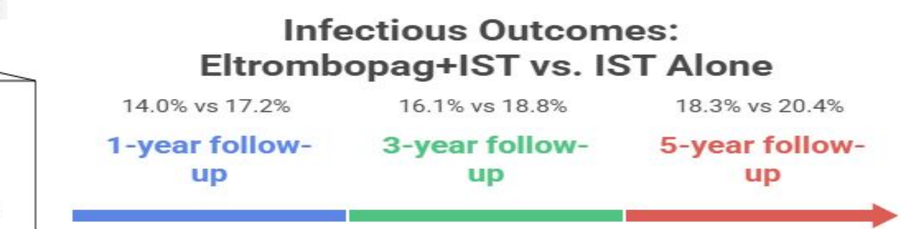




Results







- **Pneumonia risk percent in eltrombopag+IST vs IST only: 1 year (8.0% in both); 3 years (8.6 vs 8.0); 5 years (10.2 vs 10.8)**
- **No clonal evolution to AML or MDS at 1-, 3-, or 5-years in either cohort.**
- **No inpatient hospitalizations or invasive fungal infections were identified during the study period in either group.**

Conclusion

- Eltrombopag with IST demonstrated comparable long-term survival and infectious outcomes relative to IST alone, without evidence of increased clonal evolution to AML or MDS.
- No cases of AML/MDS transformation, invasive fungal infection, or inpatient hospitalization were observed across all time points.
- Infection rates consistently favored eltrombopag-based therapy.

Limitations

- Residual confounding from unmeasured variables (e.g., aplastic anemia severity, bone marrow cellularity, cytogenetic abnormalities, disease duration, treatment adherence, and performance status) may persist.
- Reliance on **EHR coding** introduces the potential for coding errors, incomplete documentation, and outcome misclassification.

Future Directions

While these findings support the long-term safety profile of eltrombopag in IAA and provide reassuring real-world evidence regarding leukemic transformation risk, they highlight the need for larger prospective studies evaluating infectious and clonal outcomes.

References

TriNetX, Real-world evidence: TriNetX platform methodology. Cambridge (MA):TriNetX LLC; 2026 (cited available from: https://trinetx.com/real-world-resources/

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