Cardiac Safety of Dasatinib, Nilotinib, and Imatinib in Chronic Myeloid Leukemia: A Real-World Propensity-Matched Comparison

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Data source: TriNetX US Collaborative Network

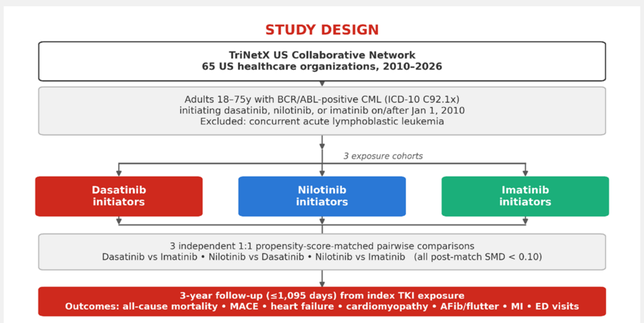
INTRODUCTION

BCR-ABL tyrosine kinase inhibitors (TKIs) are the cornerstone of chronic myeloid leukemia (CML) therapy, yet their long-term cardiovascular and mortality profiles in routine clinical practice remain incompletely characterized.

Dasatinib, nilotinib, and imatinib differ in off-target kinase inhibition and have each been linked to distinct cardiovascular safety signals in prior literature, but head-to-head real-world comparisons remain limited.

AIM / OBJECTIVE

To compare 3-year major adverse cardiovascular events (MACE), cardiac-specific outcomes, and all-cause mortality among adults with CML treated with dasatinib, nilotinib, or imatinib, using three independent propensity-matched pairwise comparisons.



METHOD

- Design: Retrospective propensity-score matched (PSM) cohort study, TriNetX US Collaborative Network (65 healthcare organizations), 2010–2026.
- Population: Adults 18–75 years with BCR/ABL-positive CML (ICD-10 C92.1x) initiating dasatinib, nilotinib, or imatinib on/after Jan 1, 2010; concurrent acute lymphoblastic leukemia excluded.
- Comparisons: three independent 1:1 PSM analyses
  - dasatinib vs imatinib (n=2,306/cohort),
  - nilotinib vs dasatinib (n=1,046/cohort),
  - nilotinib vs imatinib (n=1,413/cohort)
- PSM matched on demographics, hypertension, ischemic heart disease, heart failure, prior MI, atrial fibrillation, CKD, diabetes, dyslipidemia, smoking, and pre-index cardiac medications (all post-match standardized differences <0.10).
- Follow-up: 1–1,095 days (3 years) after first TKI exposure.
- Outcomes: all-cause mortality; composite MACE; heart failure (overall, HFrEF, HFpEF); cardiomyopathy; atrial fibrillation/flutter; myocardial infarction; ED visits. Risk ratios (z-test p) and Kaplan–Meier hazard ratios (log-rank p) estimated for each outcome.

CONCLUSIONS

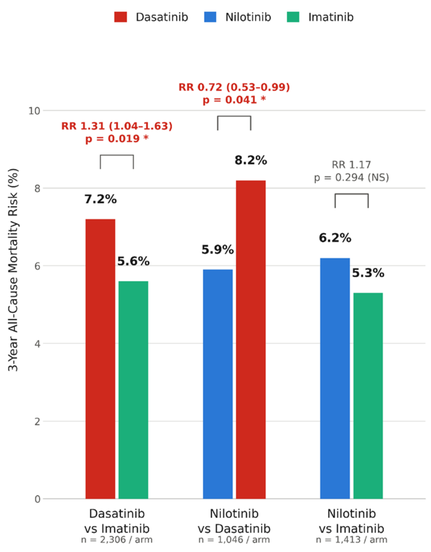
Dasatinib was associated with 28–31% higher 3-year all-cause mortality versus both imatinib and nilotinib, while cardiac-specific event rates did not differ significantly across any pairwise TKI comparison.

The mortality excess with dasatinib was not explained by the cardiac endpoints captured in this analysis, suggesting non-cardiac mechanisms (e.g., pulmonary toxicity) may contribute.

Prospective evaluation with cause-of-death adjudication is warranted before these signals inform front-line TKI selection.

RESULTS

Figure 1. Three-Year All-Cause Mortality by TKI, Across Three Propensity-Matched Pairwise Comparisons



* p < 0.05 (risk-difference z-test). RR = risk ratio; 95% CI in parentheses; NS = not significant.

KEY FINDINGS

- **Dasatinib vs imatinib: mortality 7.2% vs 5.6% (HR 1.28, 1.02–1.61, p=0.034)**
- **Nilotinib vs dasatinib: mortality 5.9% vs 8.2% (HR 0.73, 0.52–1.01, p=0.054)**
- Nilotinib vs imatinib: mortality did not differ (6.2% vs 5.3%, p=0.295)
- No significant difference for MACE, heart failure (incl. HFrEF/HFpEF), cardiomyopathy, atrial fibrillation/flutter, or MI in any of the 3 pairwise comparisons (all p>0.05)
- Mortality excess with dasatinib not explained by captured cardiac endpoints

Figure 1 (left). Three-year all-cause mortality by treatment arm, across three propensity-matched pairwise comparisons.

Table 1 (right). Full risk-ratio results for all nine outcomes across all three comparisons. RR = risk ratio; CI = confidence interval; NS = not significant (p≥0.05).

Outcome (3-yr risk)	Dasatinib vs Imatinib RR (95% CI), p	Nilotinib vs Dasatinib RR (95% CI), p	Nilotinib vs Imatinib RR (95% CI), p	Significant? (of 3 comparisons)
All-cause mortality	**1.31 (1.04–1.63), p=0.019**	**0.72 (0.53–0.99), p=0.041**	1.17 (0.87–1.58), p=0.294	**Yes (2 of 3)**
MACE composite	1.07 (0.96–1.20), p=0.242	1.10 (0.93–1.29), p=0.263	1.13 (0.97–1.31), p=0.110	No (0 of 3)
Heart failure (overall)	1.10 (0.92–1.33), p=0.301	0.83 (0.62–1.11), p=0.200	0.84 (0.65–1.09), p=0.199	No (0 of 3)
Heart failure – HFrEF	0.90 (0.66–1.23), p=0.509	0.90 (0.53–1.51), p=0.682	0.86 (0.56–1.33), p=0.501	No (0 of 3)
Heart failure – HFpEF	1.12 (0.85–1.48), p=0.419	0.93 (0.60–1.43), p=0.728	1.00 (0.67–1.50), p=1.000	No (0 of 3)
Cardiomyopathy	0.87 (0.65–1.18), p=0.380	1.08 (0.63–1.87), p=0.775	0.81 (0.52–1.26), p=0.358	No (0 of 3)
Atrial fibrillation/flutter	1.02 (0.80–1.28), p=0.899	1.20 (0.86–1.68), p=0.277	1.00 (0.75–1.34), p=1.000	No (0 of 3)
Myocardial infarction	0.91 (0.66–1.25), p=0.557	1.17 (0.72–1.89), p=0.529	1.54 (0.94–2.51), p=0.081	No (0 of 3)
Emergency department visit	1.05 (0.95–1.16), p=0.351	0.99 (0.85–1.16), p=0.916	0.98 (0.86–1.12), p=0.790	No (0 of 3)

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CONTACT INFORMATION

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REFERENCES

1. Dahlén T, Edgren G, Lambe M, et al. Cardiovascular events associated with use of tyrosine kinase inhibitors in chronic myeloid leukemia: a population-based cohort study. Ann Intern Med. 2016;165(3):161–166.

2. Montani D, Bergot E, Günther S, et al. Pulmonary arterial hypertension in patients treated by dasatinib. Circulation. 2012;125(17):2128–2137.

3. Kim TD, Rea D, Schwarz M, et al. Peripheral artery occlusive disease in chronic phase chronic myeloid leukemia patients treated with nilotinib or imatinib. Leukemia. 2013;27(6):1316–1321.

4. Data source: TriNetX, LLC. TriNetX US Collaborative Network (www.trinetx.com).