CML-1249 Rising Cardiovascular Co-mortality Among Decedents With Chronic Myeloid Leukemia in the United States, 2003-2024

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INTRODUCTION

- The advent of BCR-ABL1 tyrosine kinase inhibitors (TKIs) transformed chronic myeloid leukemia (CML) from a fatal hematologic malignancy into a chronic survivorship condition with near-normal life expectancy.
- Prolonged survival combined with aging, baseline cardiovascular risks, and class-specific vascular/metabolic toxicities of sequential TKIs has shifted the mortality profile toward competing non-leukemic causes.
- Population-level evaluation of nationwide Multiple Cause of Death records clarifies long-term cardiovascular mortality trajectories across 22 years of the TKI era.

AIM

Primary Aim: Quantify national 22-year trajectories (2003–2024) of cardiovascular (CV) co-mortality among CML-associated decedents.

Secondary Aim: Characterize component-specific shifts (ischemic heart disease, heart failure, cerebrovascular disease, hypertension) and evaluate temporal trends across early vs. contemporary TKI eras (2003–2010 vs. 2011–2024).

METHOD

Data Source: CDC WONDER / NCHS Multiple Cause of Death files (2003–2024) identifying decedents with CML (ICD-10 C92.1) in underlying or contributing cause fields.

Cardiovascular Definitions:
Core CV: Hypertensive disease (I10–I15), ischemic heart disease (I20–I25), and cerebrovascular disease (I60–I69).
Expanded CV: Core CV plus heart failure (I50) and atherosclerotic/peripheral vascular disease (I70–I73).

Statistical Analysis: Multivariable binomial logistic regression modeling annual odds of CV co-mention and piecewise regression with an inflection knot at 2010 (capturing second-generation TKI frontline expansion).

CONCLUSIONS

- Cardiovascular disease represents an escalating contributor to mortality among patients with CML, now co-mentioned in **more than 1 in 4** (core) and **over 1 in 3** (expanded) decedents nationwide.
- The marked rise in heart failure, hypertension, and ischemic heart disease underscores the necessity of integrated cardio-oncology surveillance, proactive vascular risk mitigation, and personalized TKI selection in long-term survivorship.

RESULTS

National Cohort (N=34,831): Evaluated 11,223 CML decedents in the early TKI era (2003–2010) and 23,608 in the contemporary TKI era (2011–2024).

Rising Cardiovascular Co-Mortality:

Core CV: Increased from **15.0% to 26.4%** (OR **1.025**/yr, 95% CI 1.021–1.029, $p < 0.001$; era means: 17.9% vs. 21.7%).

Expanded CV: Increased from **21.5% to 36.4%** (era means: 24.7% vs. 31.2%).

Component-Specific Drivers:

Heart Failure: Nearly doubled from **8.1% to 15.8%** (era means: 8.9% to 13.4%).

Hypertension & Stroke: Hypertension rose from 0.4% to **8.4%**; stroke rose from 3.8% to **6.2%**.

Ischemic Heart Disease: Increased from 11.4% to **15.5%**, while acute MI declined modestly (3.0% to 2.2%).

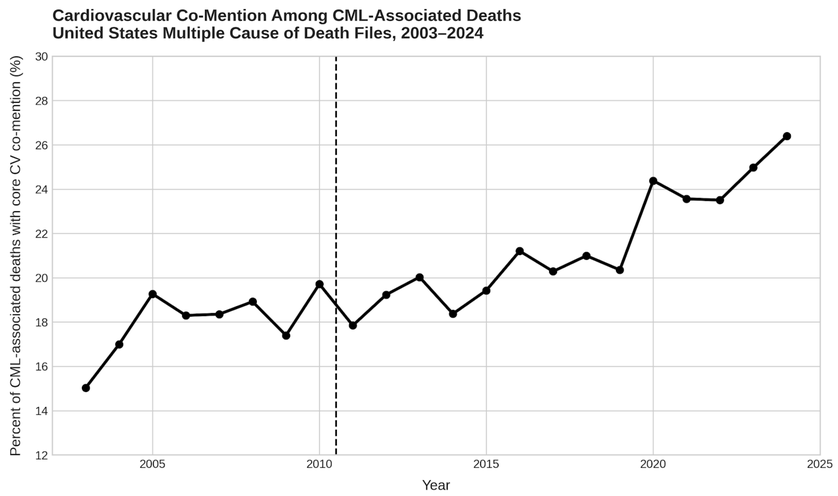

Figure 1. 22-Year Trajectory of Cardiovascular Co-Mention Among CML-Associated Decedents (2003–2024). Annual proportion of nationwide CML deaths co-mentioning core cardiovascular disease from NCHS Multiple Cause of Death records. Dashed vertical line at 2010 denotes the introduction and expanded frontline approval of second-generation TKIs. Core CV co-mortality increased from 15.0% in 2003 to 26.4% in 2024, with more than 1 in 3 decedents dying with expanded cardiovascular disease in the modern era.

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