A 24-Year Analysis of Chronic Myeloid Leukemia (CML) Mortality in the US: Shifts Across Pre-TKI, Early TKI, and Modern TKI Eras

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Background

Chronic Myeloid Leukemia (CML) is a hematologic malignancy driven by the BCR-ABL1 fusion gene. Prognosis has drastically improved since the introduction of tyrosine kinase inhibitors (TKIs), beginning with imatinib in 2001. These therapies have transformed CML into a chronic, manageable disease with near-normal life expectancy. However, recent reports suggest a slowing of mortality improvements, possibly due to resistance, long-term toxicity, or disparities in access and adherence.

Aim

This study aims to explore changes in trends and patterns in CML mortality stratified by demographic variables and geographic regions in the US from 1999 to 2023, in the pre-TKI, early TKI, and late TKI eras.

Methods

We used the CDC-WONDER database to extract age-adjusted mortality rates (AAMRs) per 1,000,000 individuals. AAMRs were analyzed using the Joinpoint Regression Program to evaluate annual percentage changes (APCs) and average annual percentage changes (AAPCs) in mortality. The study duration was divided into three eras: pre-TKI (1999-2001), early TKI (2002-2010), and modern TKI (2011-2023).

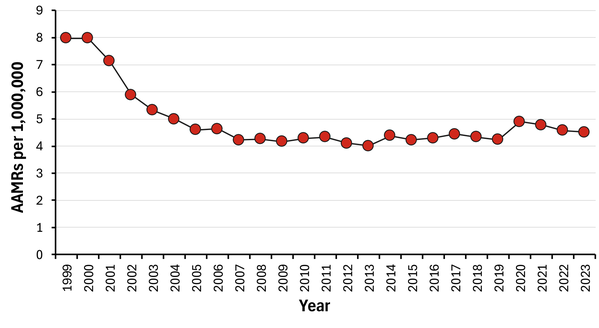
Discussion

The observed significant decline in CML mortality during the pre-TKI and early TKI eras aligns with historical evidence of imatinib's transformative impact, where population-based studies documented mortality reductions of 70–80% post-introduction.[1] The plateau in the modern TKI era (2011–2023) may reflect emerging challenges, including treatment-resistant mutations, cardiovascular toxicities from newer TKIs, and demographic shifts toward older patients with comorbidities.[2] Persistent male-female disparities (males: 2× higher mortality) likely stem from higher cardiovascular risk profiles in males and sex-specific pharmacokinetics affecting TKI efficacy.[2] Racial inequities, notably higher mortality in non-Hispanic Blacks, highlight systemic gaps in healthcare access, timely diagnosis, and optimal monitoring, consistent with SEER-based analyses.[3] The attenuated decline in recent years underscores the need for enhanced cardio-oncology surveillance to mitigate disparities and sustain the progress.

Results

From 1999 to 2023, CML caused 40,941 deaths, showing a decreasing trend [APC: -2.30% (-2.71 to -1.87)]. The AAMR was 7.7 (7.51 to 7.89) during the pre-TKI era, 4.68 (4.60 to 4.76) during the early TKI era, and 4.39 (4.18 to 4.61) during the modern TKI era. The decline in mortality was the highest during the pre-TKI era [APC: -8.33% (-9.69 to -6.95)], followed by the early TKI era [APC: -4.99% (-5.84 to -4.13)]. The modern TKI era showed a smaller, non-significant increase with an APC of 0.85%. Males exhibited a slightly greater decline than females in the pre-TKI era (-9.1% vs. -8.83%), while females exhibited a slightly greater decline in the early TKI (-5.36% vs. -4.38%) and modern TKI era (0.73% vs. 0.59%). Males experienced twice the mortality burden as that of females during all three eras [(10.11 vs. 5.93), (6.28 vs. 3.53), and (5.89 vs. 3.24), respectively]. Non-Hispanic Asians showed the lowest burden (5.17, 2.59, 2.21) and the highest decline (-14.54%, -5.77%, -0.09%) throughout the three eras, while non-Hispanic blacks showed the highest burden (8.28, 5.20, 4.28). Non-Hispanic blacks experienced the lowest decline (-8.20%) in pre-TKI and non-Hispanic whites (-4.22%) in the early TKI era.

Trends in Chronic Myeloid Leukemia Mortality in the US,1999-2020



Conclusion

CML mortality in the US declined from 1999 to 2023, with the most pronounced reduction during the pre-TKI and early TKI eras. However, the decline plateaued in the modern TKI era, with a slight increase observed.

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The authors declare no conflict of interest

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