Cumulative Imatinib Exposure is associated with Renal but Not Skeletal Dysfunction in Chronic Phase CML

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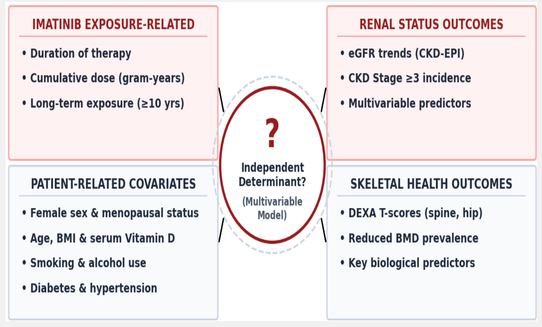
INTRODUCTION

- Tyrosine kinase inhibitors (TKIs) have transformed chronic myeloid leukemia (CML) into a long-term survivorship disease.
- As patients live decades beyond diagnosis, outcomes beyond molecular response are critical.
- Imatinib has been associated with renal and skeletal changes, but whether these reflect cumulative exposure or patient characteristics remains uncertain.

AIM

- To assess Imatinib exposure-related versus patient-related determinants of renal function and bone mineral density (BMD) in chronic phase CML patients achieving treatment milestones.



METHOD

- **Design**: Cross-sectional study at King George's Medical University, Lucknow, India
- **Population**: 600 chronic-phase CML patients exclusively treated with imatinib, including 124 newly diagnosed, imatinib-naïve controls.
- **Imatinib Exposure groups**: *Controls (n=124), 1–5 years (n=231),5–10 years (n=131), and ≥10 years (n=114).*
- **Outcomes:** Renal function (eGFR, CKD ≥stage 3) and skeletal status (WHO-defined osteopenia/osteoporosis).
- **Analysis:** Multivariable regression adjusted for age, sex, menopausal status, BMI, Hypertension, Diabetes, Calcium, Phosphorus, and Vitamin D levels in serum; cumulative exposure expressed as gram-years.

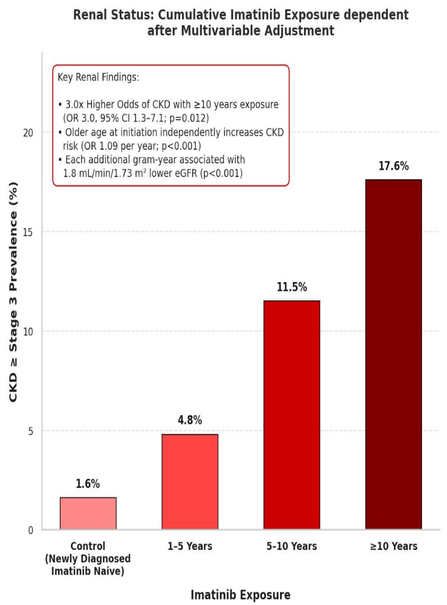
CONCLUSIONS

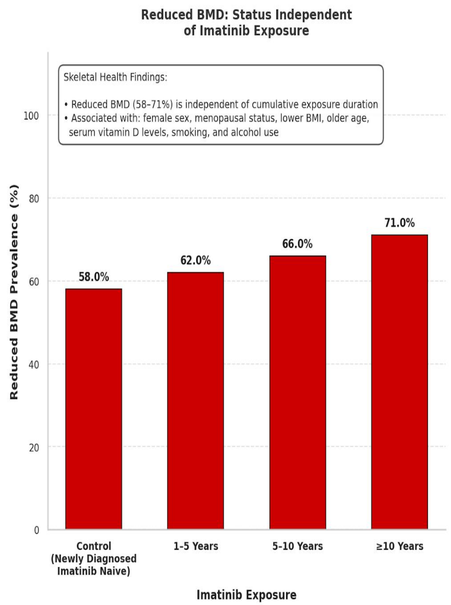
- ***In this cross-sectional cohort, renal dysfunction was associated with cumulative imatinib exposure, whereas reduced BMD was driven predominantly by patient-related risk factors.***
- ***These findings support routine longitudinal renal surveillance in patients receiving prolonged imatinib therapy and suggest that bone-health assessment should be individualized according to baseline risk factors.***

RESULTS

- ***CKD ≥ stage 3:*** *47 patients (7.9%); prevalence increased with imatinib duration:* ***1.6% → 4.8% → 11.5% → 17.6%*** *across controls, 1–5, 5–10, and ≥10 years, respectively.*
- ***Prolonged exposure:*** *≥10 years of imatinib independently increased CKD odds 3-fold (OR 3.0, 95% CI 1.3–7.1; p=0.012) after multivariable adjustment.*
- ***Age at initiation:*** *Each additional year of age at imatinib initiation independently increased CKD risk by 9% (OR 1.09; p<0.001).*
- ***Cumulative Imatinib exposure*:*** *Each additional gram-year of imatinib exposure was independently associated with a 1.8 mL/min/1.73 m² lower eGFR (p<0.001).*
- ***Bone Health:*** *Reduced BMD (58–71%) was associated with menopausal status, female sex, lower BMI, and older age, but not to cumulative imatinib exposure.*

* Cumulative imatinib exposure (g-years) = daily dose (g) × actual treatment duration (years), accounting for treatment interruptions.





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