# Asciminib Versus Dasatinib/Nilotinib as First-Line Tyrosine Kinase Inhibitor Therapy in Chronic Myeloid Leukemia: A Propensity Score-Matched Analysis of Disease Progression and Safety Outcomes

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SOHO 2026 · Abstract #913 · Chronic Myeloid Leukemia (CML)

## INTRODUCTION

- Asciminib targets the ABL myristoyl pocket, bypassing the ATP-binding site used by dasatinib and nilotinib.[1]
- The phase 3 ASC4FIRST trial demonstrated superior 48-week major molecular response (MMR) rates for asciminib versus investigator-selected TKIs (**67.7% vs. 49.0%**).[2,3]
- Real-world comparative data against second-generation TKIs remain limited.

## AIM

To compare disease progression and safety outcomes between asciminib and dasatinib/nilotinib as first-line TKI therapy in chronic myeloid leukemia (CML) using real-world data.

## METHODS

- **Data source.** TriNetX Research Network — 112 healthcare organizations, approximately 147.5 million patients.[4]
- **Population.** Adults with BCR-ABL–positive CML initiating asciminib (n=327) or dasatinib/nilotinib (n=5,789) as their only TKI within 90 days of diagnosis.
- **Matching.** Propensity score matching (1:1) on age, sex, race, ethnicity, diabetes, chronic kidney disease, heart failure and hepatic fibrosis/cirrhosis yielded 315 patients per cohort.
- **Primary endpoint.** Disease progression between days 90 and 270, defined as escalation to ponatinib or omacetaxine, hematopoietic stem cell transplantation, or transformation to acute leukemia.
- **Secondary safety outcomes.** Cytopenia, pleural effusion, cardiovascular events and pancreatitis.
- Outcomes were extracted from structured EHR data without manual chart review.

## CONCLUSIONS

- **The cytopenia reduction with asciminib was substantial and statistically significant.**
- The progression difference did not reach statistical significance, partly reflecting insufficient power to detect a moderate effect.
- Retrospective claims-level ascertainment of progression is imperfect, as some therapy switches may not represent true disease advancement.
- **The safety profile represents the most defensible argument for asciminib in the frontline setting** — a consideration of particular relevance when managing a largely chronic disease population.

## RESULTS

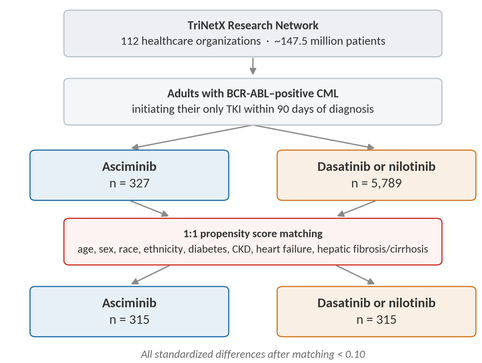



*Figure 1. Cohort selection and propensity score matching.*

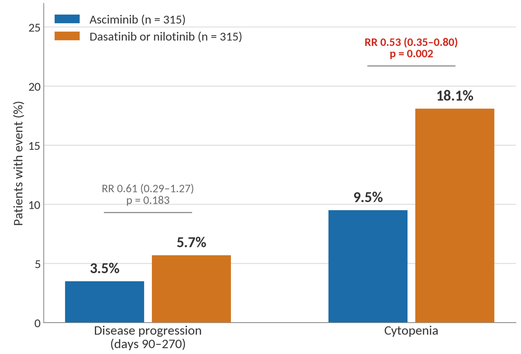



*Figure 2. Event rates by cohort. Cytopenia differed significantly; progression did not.*

### KEY RESULTS

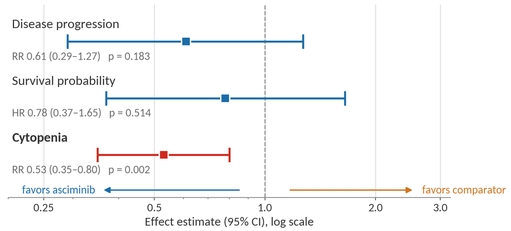
- Post-matching balance was acceptable across all covariates (standardized differences < 0.10).
- Eleven asciminib patients (3.5%) progressed versus 18 (5.7%) in the comparator cohort — RR 0.61 (95% CI 0.29–1.27), p = 0.183.
- Survival probabilities were 94.5% versus 93.4% — HR 0.78 (95% CI 0.37–1.65), log-rank p = 0.514.
- **Cytopenia occurred in 9.5% versus 18.1% — RR 0.53 (95% CI 0.35–0.80), p = 0.002.**
- Pleural effusion and cardiovascular events were rare in both groups, with cell counts too low for meaningful subgroup analysis. No pancreatitis events were recorded in either cohort.

**Table 1. Progression and safety outcomes in the matched cohorts.**

| Outcome | Asciminib (n = 315) | Dasatinib or nilotinib (n = 315) | Effect estimate (95% CI) | p |
|---|---|---|---|---|
| Disease progression, days 90–270 | 11 (3.5%) | 18 (5.7%) | RR 0.61 (0.29–1.27) | 0.183 |
| Survival probability (Kaplan-Meier) | 94.5% | 93.4% | HR 0.78 (0.37–1.65) | 0.514 |
| **Cytopenia** | **9.5%** | **18.1%** | **RR 0.53 (0.35–0.80)** | **0.002** |
| Pleural effusion | rare* | rare* | — | — |
| Cardiovascular events | rare* | rare* | — | — |
| Pancreatitis | 0 | 0 | — | — |

** Rare in both groups; cell counts too low for meaningful subgroup analysis.*

*Figure 3. Effect estimates with 95% confidence intervals.*




## LIMITATIONS

- Retrospective claims-level ascertainment of progression is imperfect, as some therapy switches may not represent true disease advancement.
- The comparison had insufficient power to detect a moderate effect on disease progression.
- Pleural effusion and cardiovascular events were rare in both groups, with cell counts too low for meaningful subgroup analysis.
- Outcomes were extracted from structured EHR data without manual chart review.

## REFERENCES

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## CONTACT & ACKNOWLEDGEMENTS

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This analysis used de-identified electronic health record data from the TriNetX Research Network. The authors thank the participating healthcare organizations. This abstract was not industry supported.