EFFICACY AND SAFETY OF ASCIMINIB IN CHRONIC MYELOID LEUKEMIA AFTER TYROSINE KINASE INHIBITOR FAILURE: A SYSTEMATIC REVIEW AND META-ANALYSIS

B. Fernandes[1], W. Fernandes[2], V. Shah[1], C. Dirican[1], S.H. Narayana[1], M.A. Ali[3], W. Aiman[4], A.V. Ganesan[1], F. Ajayi[5], G. Guron[5], M. Maroules[1]

[1] New York Medical College Graduate Medical Education Program at St. Mary's General Hospital and Saint Clare's Health, Denville, NJ, USA
[2] Saint Vincent Hospital, Worcester, MA, USA
[3] Allegheny Health Network Cancer Institute, Pittsburgh, PA, USA
[4] Roswell Park Cancer Center, University of Buffalo, Buffalo, NY, USA
[5] New York Medical College / St. Michael's Medical Center, Newark, NJ, USA

NEW YORK MEDICAL COLLEGE
A MEMBER OF TOURO UNIVERSITY
School of Medicine

Introduction

- Tyrosine kinase inhibitors (TKIs) have transformed the management of chronic myeloid leukemia (CML).
- Resistance or intolerance to multiple TKIs remains a major clinical challenge.
- Asciminib is a first-in-class STAMP inhibitor (Specifically Targeting the ABL Myristoyl Pocket) with a unique mechanism of action.
- Individual studies suggest promising outcomes, but pooled evidence on efficacy and safety is limited.

Aim

- To evaluate the clinical efficacy and safety of asciminib in patients with chronic-phase CML after failure of ≥2 TKIs.

Objectives

- Assess molecular and cytogenetic response rates (MMR, CCyR, CHR).
- Evaluate survival outcomes (OS).
- Summarize safety data, including grade ≥3 AEs and arterial occlusive events.

Methods

- Search strategy: PubMed, Embase, and ClinicalTrials.gov.
- Records identified: 310; included studies: 23 (clinical trials + real-world data).
- Population: Adults with chronic-phase CML, post ≥2 TKIs.
- Intervention: Asciminib monotherapy.
- Efficacy: Major Molecular Response (MMR), Complete Cytogenetic Response (CCyR), Complete Hematologic Response (CHR)
- Safety: Overall Survival (OS), grade ≥3 Adverse Events (AEs), Arterial Occlusive Events
- Analysis: Random-effects model (R software).

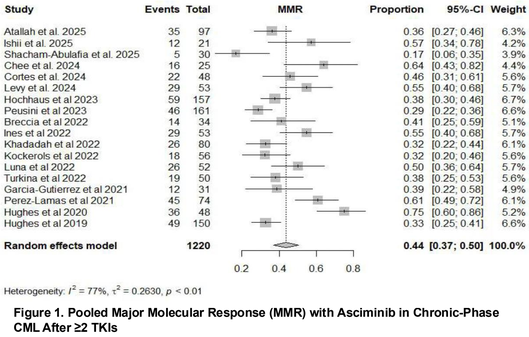


Figure 1. Pooled Major Molecular Response (MMR) with Asciminib in Chronic-Phase CML After ≥2 TKIs

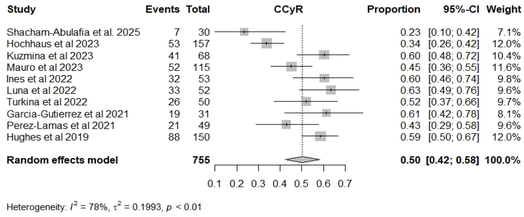


Figure 2. Pooled Complete Cytogenetic Response (CCyR) with Asciminib in Chronic-Phase CML After ≥2 TKIs

Results

EFFICACY

- MMR: 44% (95% CI 37–50%; I² = 77%)
- CCyR: 50% (95% CI 42–58%; I² = 78%)
- CHR: 63% (95% CI 24–90%; I² = 94%)

SAFETY

- Overall Survival: 89% (95% CI 78–95%; I² = 87%)
- Grade ≥3 AEs: 27% (95% CI 18–39%; I² = 93%)
- Arterial occlusive events: 5% (95% CI 3–9%; I² = 27%)

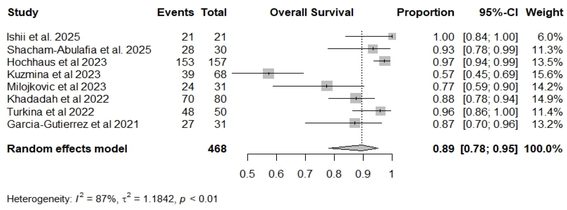


Figure 3. Pooled Overall Survival (OS) with Asciminib in Chronic-Phase CML After ≥2 TKIs

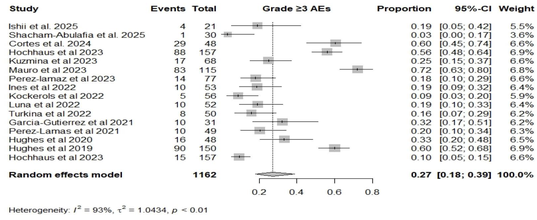


Figure 4. Forest plot of pooled Grade ≥3 Adverse Events (AEs) with Asciminib in Chronic-Phase CML After ≥2 TKIs

Summary

Asciminib provides meaningful efficacy with an acceptable safety profile in chronic-phase CML after ≥2 prior TKIs, supporting its role as a key option in relapsed or refractory settings.

Discussion

- Our findings confirm that asciminib provides meaningful molecular and cytogenetic responses in chronic-phase CML after failure of ≥2 TKIs, addressing a critical unmet need in this population.
- Although grade ≥3 AEs were observed in ~27% of patients, arterial occlusive events were infrequent (5%), supporting an overall favorable safety profile compared with historical TKI data.
- The pooled efficacy outcomes (MMR 44%, CCyR 50%) compare favorably with third-line TKI options, reinforcing asciminib's potential role as a preferred therapy in resistant/refractory settings.
- Longer follow-up and prospective real-world studies are needed to determine durability of response, optimize sequencing, and better define patient selection for asciminib.

References

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SOHO2025