SOHO ANNUAL MEETING 2026

Efficacy and Safety of Asciminib As Second-Line or Later Therapy in Chronic-Phase Chronic Myeloid Leukemia: An Updated Systematic Review and Meta-Analysis

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INTRODUCTION

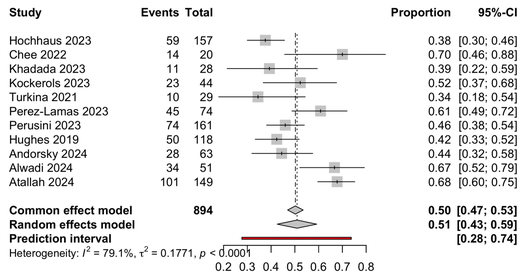
- Chronic myeloid leukemia in chronic phase (CML-CP) patients who develop resistance or intolerance to prior tyrosine kinase inhibitors (TKIs) remain a major therapeutic challenge, particularly in later-line settings.
- Asciminib, a first-in-class Specifically Targeting the ABL Myristoyl Pocket (STAMP) inhibitor, represents a novel therapeutic strategy for previously treated CML-CP.
- A prior meta-analysis by Fan et al. reported a pooled major molecular response (MMR) rate of approximately 47% with asciminib beyond first-line therapy.
- Since that publication, additional clinical and real-world studies have become available, including studies evaluating earlier-line use of asciminib.

METHODS

- **Study objective:** To provide updated pooled estimates of the efficacy and safety of asciminib as second-line or later therapy for chronic myeloid leukemia in chronic phase (CML-CP) and evaluate the influence of treatment line on molecular response.
- **Study design:** Systematic review and meta-analysis conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.
- **Literature search:** PubMed, EMBASE, Web of Science, and Cochrane Library were searched through October 2025.
- **Eligibility:** Studies including adult patients with CML-CP receiving asciminib as second-line or later therapy and reporting molecular response or safety outcomes were eligible.
- **Study types:** Randomized trials, comparative studies, and observational cohorts were included.
- **Primary outcome:** Pooled major molecular response (MMR).
- **Secondary outcomes:**
  - MR4
  - Grade ≥3 adverse events (AEs)
- **Subgroup analysis:** Molecular response was compared between second-line therapy (2L) and third-line or later therapy (≥3L).

RESULTS

- **Study selection:** 11 studies comprising 894 patients were included: 1 randomized trial, 1 nonrandomized comparative study, 9 observational cohorts
- **Follow-up:** Median follow-up ranged from 12–26 months.
- **Major molecular response (MMR):**
  - Pooled MMR rate was 51% (95% CI, 43–59%; $I^2 = 79\%$).
  - This was numerically higher than the 46.9% reported by Fan et al. in the previous meta-analysis.
  - The 95% prediction interval was 0.28–0.74, indicating substantial between-study variability.
- **Treatment-line subgroup analysis:**
  - Second-line (2L): 60% MMR
  - Third-line or later (≥3L): 47% MMR
  - Difference did not reach statistical significance (p = 0.0569).
- **Deep molecular response (MR4):**
  - MR4 was achieved in 30% of patients (95% CI, 23–37%; $I^2 = 78\%$), compared with 26.7% reported by Fan et al.
- **Safety:**
  - Grade ≥3 adverse events (AEs) occurred in 30% of patients (95% CI, 14–52%; $I^2 = 95\%$), compared with 39.5% reported by Fan et al.
- **Sensitivity analysis:** Pooled estimates remained robust after exclusion of individual studies.
- **Publication bias:** No significant evidence of publication bias was identified (Egger regression, p = 0.67).



Forest plot of pooled MMR with random-effects model

CONCLUSIONS

- **Asciminib demonstrates clinically meaningful molecular responses in previously treated CML-CP, with numerically higher MMR in the second-line setting.**
- **However, this difference was not statistically significant. Prospective comparative studies are warranted to clarify the optimal treatment line for asciminib.**

Acknowledgements

- **Dr. Meenal Mohgaonkar,** Professor of Radiology and Director Academics at SMBT IMS & RC, Nashik, India
- **Dr. Manasi Padhyegurjar** Professor of community medicine and Dean at and Director Academics at SMBT IMS & RC, Nashik, India
- **Dr. Sandip Lambe,** Professor of Biochemistry and Deputy Dean at SMBT IMS & RC, Nashik, India

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