Asciminib Monotherapy in Chronic Myeloid Leukaemia: A Systematic Review of Efficacy and Safety from Phase 1-3 Trials

Trials

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Introduction

Although the ATP-competitive tyrosine kinase inhibitors (TKIs) brought transformative success in chronic myeloid leukaemia (CML), long-term management remains challenged by resistance, intolerance, and off-target toxicity (1). Asciminib, a STAMP inhibitor that allosterically targets the ABL myristoyl pocket, offers a novel therapeutic approach. This review summarizes the efficacy and safety of asciminib monotherapy across treatment lines, including newly diagnosed, multi-TKI-resistant, and T315I-mutated chronic-phase CML (CML-CP).

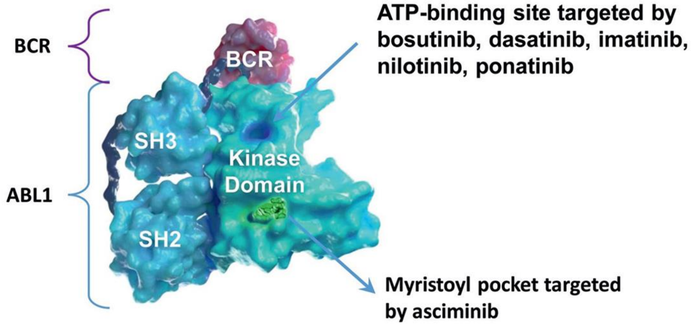


Figure 1. Site of action of TKIs and Asciminib (2)

Methods

We conducted a structured literature search to identify Phase 1-3 interventional trials published or presented through May 2025. These studies assessed efficacy (e.g., major molecular response [MMR]) and safety in patients receiving asciminib as monotherapy.

MOA of Asciminib

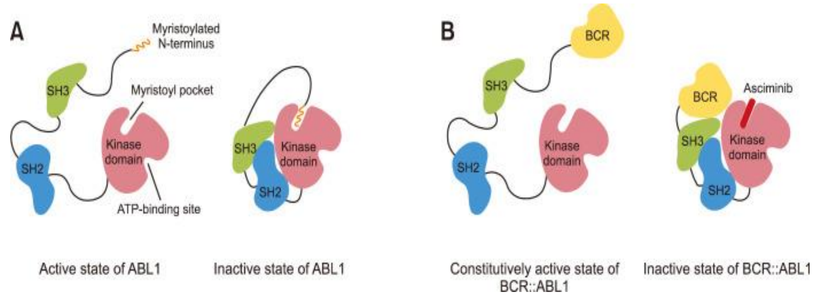


Figure 2. A) Normal conditions, ABL1 activity is autoregulated. B) In CML, we find that Asciminib binds to the myristoyl pocket of the ABL1 kinase domain, and hence inhibits kinase activity(3)

Results

Ten studies met the inclusion. In heavily pretreated CML-CP, the ASCEMBL trial showed superior MMR at 96 weeks with asciminib versus bosutinib (37.6% vs 15.8%), as well as reduced discontinuation and grade >3 toxicity(4). In the newly diagnosed setting, the ASC4FIRST trial demonstrated superior MMR at 48 weeks compared to investigator-selected TKIs (67.7% vs 49.0%; $p < 0.001$), with fewer severe adverse events (5). In patients with T3151 mutations, asciminib 200 mg BID yielded nearly 49% MMR at 2 years, with higher rates in ponatinib-naive patients (6). A four-year Phase 1 update confirmed durable molecular responses and a low rate of vascular toxicity in patients with >2 prior TKIs. Real-world outcomes were consistent with trial efficacy. Grade >3 adverse events were uncommon, mainly involving asymptomatic lipase elevation, cardiovascular events, and thrombocytopenia.

Conclusion

Asciminib demonstrates robust molecular responses and a favourable safety profile across diverse CML-CP populations. These findings support its integration not only as a frontline option but also as a valuable agent in TKI-resistant and mutation-driven CML, with ongoing trials exploring optimal sequencing and treatment-free remission strategies.

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