Systematic Review of Front-Line Tyrosine Kinase Inhibitors for Chronic Myeloid Leukemia

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Background

- Majority of patients with chronic myeloid leukemia (CML) are identified by a translocation between chromosomes 9 and 22 in leukemic cells and are categorized as being Philadelphia chromosome positive (Ph+). This translocation causes the ABL1 gene on chromosome 9 and BCR gene on chromosome 22 to create a fusion oncogene known as BCR-ABL.
- The introduction of BCR-ABL tyrosine kinase inhibitors has improved CML management, leading to increased overall survival.
- Choosing a tyrosine kinase inhibitor (TKI) requires consideration of established efficacy, side effect profile, patient comorbidities, financial toxicity, and long-term treatment goals.

Objectives

1. Compare the efficacy and safety of BCR-ABL tyrosine kinase inhibitors in CML
2. Identify patient factors and medication specific considerations that impact tyrosine kinase selection in front line therapy

Methods

- Systematic review of PubMed and other resources was conducted to identify key clinical trials supporting BCR-ABL tyrosine kinase inhibitor approvals in front line CML, comparative efficacy data among TKIs, adverse events (AE), and specific literature addressing treatment selection criteria.

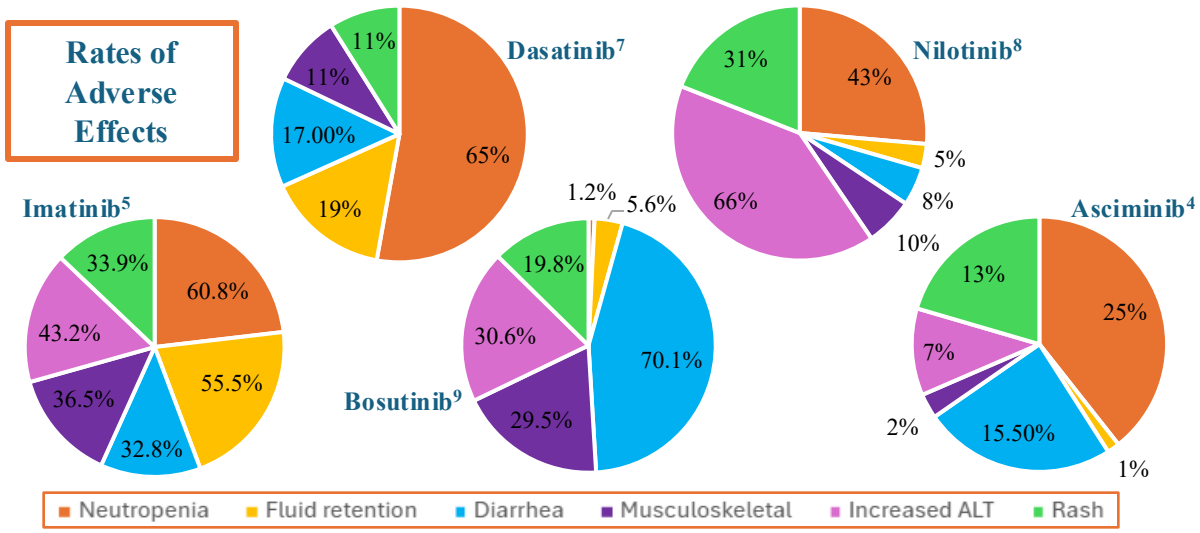
Results

TKI Efficacy Rates in Landmark Trials

Trial/TKI	CCYR		MMR		Time of median follow up
	TKI	Imatinib	TKI	Imatinib	
Dasision[1] Dasatinib	^94%	^92%	76%	64%	5 years
ENESTnd[2] Nilotinib	-	-	78%	63%	10 years
BFORE[3] Bosutinib	83%	77%	74%	65%	5 years
ASC4FIRST[4] Asciminib	84%	62%	69%	40%	16 months
	*90%	*83%	*66%	*58%	

^Achieved BCR-ABL1 transcript level ≤ 10% at 3 months
*Versus 2nd generation TKI
CCYR: Complete Cytogenic Response; MMR: Major molecular Response

Rates of Adverse Effects



Discussion

- Real-world TKI selection depends on patient specific factors (cost, comorbidities, side effects), provider familiarity, institutional guidelines, and clinical trial eligibility.
- Newer generation TKIs achieve faster, deeper responses with better tolerability, with asciminib trending to be more favorable.
- Patients seeking treatment free remission (TFR) would benefit from use of 2nd generation TKIs or later.
- Toxicity profiles of TKIs have unique differences and should guide treatment selection.
- Asciminib is attractive for older patients due to low rates of serious AEs, while imatinib still remains widely used for its low cost and accessibility.
- Newer agents, while efficacious, can carry larger financial burdens for the patient. Insurance coverage and copay cost are major determinants of frontline treatment, despite a patient being a better fit for a newer generation TKI.[15]
- With more generics emerging, we can anticipate improved patient access of newer generation TKIs.

Conclusion

- Shared decision making and identifying the best TKI for a patient remain top priorities in frontline CML treatment selection.
- Maximizing initial molecular response to achieve TFR eligibility faster can have long-term benefits like improving financial burden and toxicity associated with long-term TKI usage.

Additional Materials & References