Real-World Patterns of Tyrosine Kinase Inhibitor Discontinuation and Reinitiation in Chronic Myeloid Leukemia Patients in the United States

Jyotirmoy Sarker, Aaron N Winn

Department of Pharmacy Systems, Outcomes and Policy, Retzky College of Pharmacy, University of Illinois Chicago

BACKGROUND and AIMS

- Tyrosine kinase inhibitors (TKIs) have enhanced survival in chronic myeloid leukemia (CML) by enabling deep molecular responses (DMR).
- However, prolonged TKI use can lead to financial burdens and adverse effects.
- Discontinuation of TKIs after achieving sustained DMR may help mitigate these issues, but real-world data on discontinuation and reinitiation patterns, particularly in the United States, are limited.
- To explore real-world TKI discontinuation and reinitiation patterns among CML patients in the United States.

METHODS

- We used the Merative MarketScan Commercial Claims and Medicare Supplemental databases for this retrospective cohort study.
- Patients who initiated TKI therapy between 2010 and 2018 and maintained continuous treatment for three years were included.
- We used Kaplan-Meier estimates to assess the cumulative incidence of TKI discontinuation and reinitiation.
- We conducted Cox proportional hazards analyses, both unadjusted and adjusted, to evaluate the effects of potential factors, including age, sex, frailty, comorbidity, time on TKIs and TKI type, on discontinuation and reinitiation.

Fig 1a: Study design: time to TKI discontinuation study

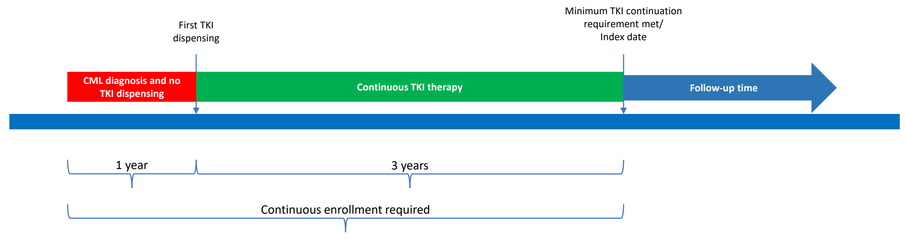


Fig 1b: Study design: time to TKI reinitiation study

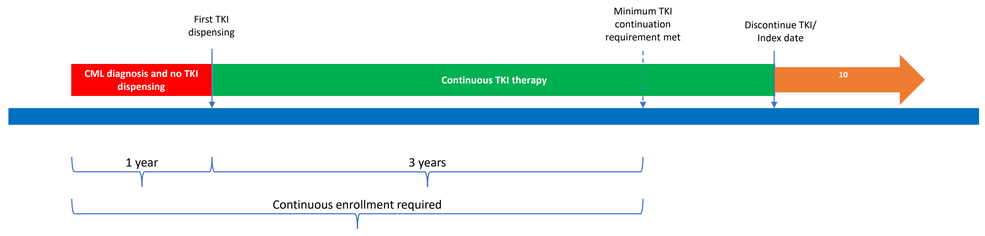


Fig 2: Cohort attrition diagram

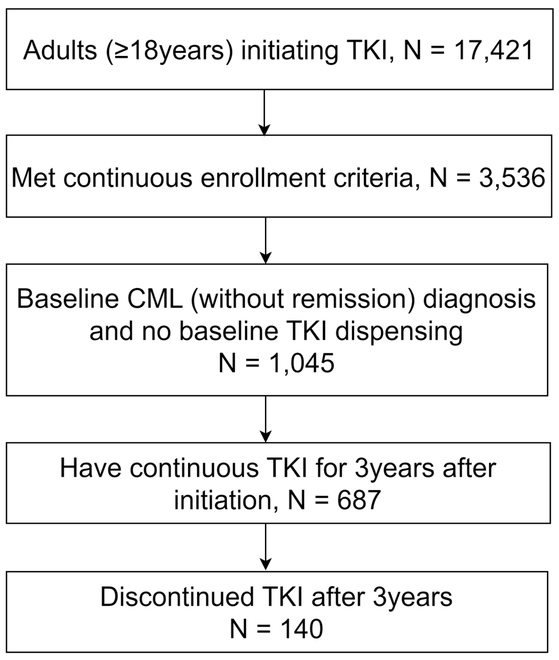


Fig 3: Cumulative incidence of discontinuation

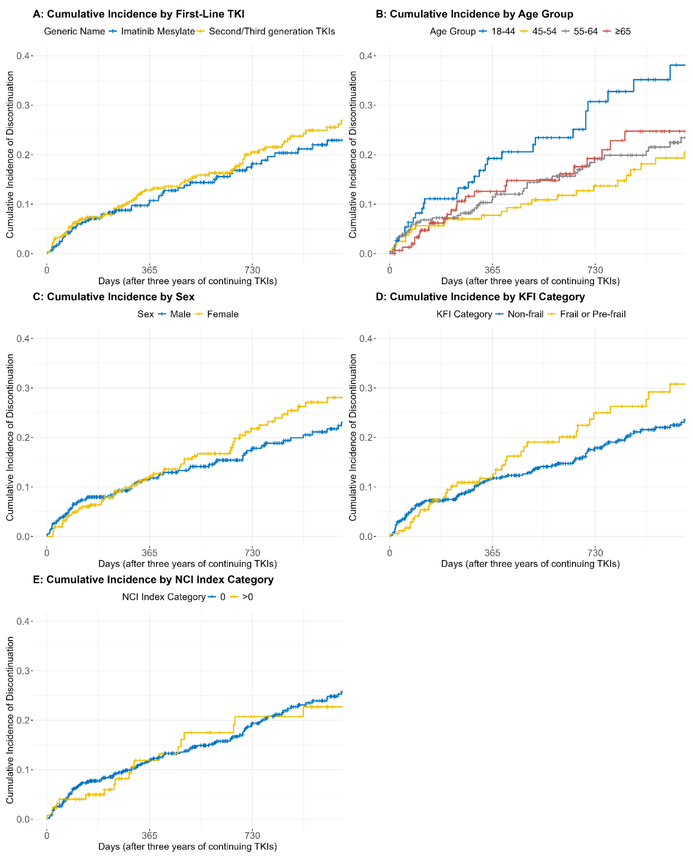
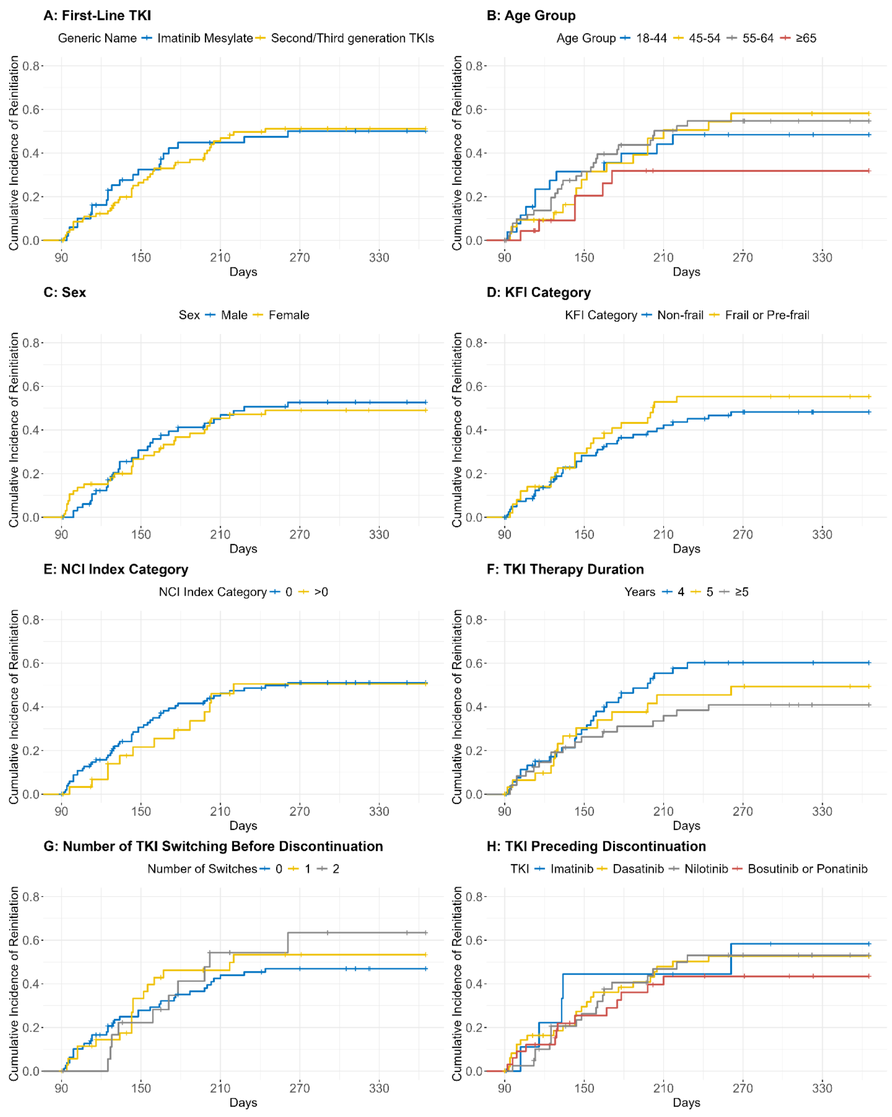


Fig 4: Cumulative incidence of TKI reinitiation



RESULTS

- 687 patients met the enrollment criteria.
- The cumulative incidence of TKI discontinuation was 11.77% after one year and 19.55% after two years.
- Discontinuation was more frequent in younger patients, frail individuals, and those using second/third-generation TKIs.
- Among those who discontinued (n=140), 50.85% reinitiated therapy within nine months.
- Cox regression analysis revealed that younger patients and frail individuals had a significantly higher risk of discontinuation compared to older, non-frail individuals.
- Time on TKI therapy appeared to be a contributing factor in the time to reinitiation analysis.

Table 1: Characteristics of patients

Characteristics		Eligible to Discontinue	Discontinuers
N		687	140
Age (years), median (IQR)		58 (49, 64)	57 (48, 62)
Age group (years), n (%)			
	18 to 44	113 (16.45)	28 (20.00)
	45 to 54	162 (23.58)	33 (23.57)
	55 to 64	256 (37.26)	56 (40.00)
	≥65	156 (22.71)	23 (16.43)
Sex (male), n (%)		379 (55.17)	71 (50.71)
NCI comorbidity index			
	0	564 (82.10)	108 (77.14)
	>0	123 (17.90)	32 (22.86)
Kim's Frailty Index			
	Non-frail	510 (74.24)	90 (64.29)
	Pre-frail or Frail	177 (25.76)	50 (35.71)
1st Line TKI			
	Imatinib	293 (42.65)	54 (38.57)
	2nd generation	394 (57.35)	86 (61.43)

Table 2: Adjusted analysis of time to TKI discontinuation and time to reinitiation

		Discontinuation	Reinitiation
		Adjusted HR (95% CI)	
First line TKIs			
	Imatinib	Reference	
	Second generation TKIs	1.12 (0.78 - 1.63)	1.04 (0.54 - 1.99)
Age group (years)			
	18-44	Reference	
	45-54	0.44 (0.25 - 0.75)	1.30 (0.59 - 2.85)
	55-64	0.53 (0.33 - 0.87)	1.23 (0.58 - 2.59)
	≥65	0.57 (0.32 - 1.01)	0.50 (0.18 - 1.42)
Sex			
	Male	Reference	
	Female	1.18 (0.82 - 1.69)	1.00 (0.59 - 1.71)
Frailty (Kim's Frailty Index)			
	Non-frail	Reference	
	Pre-frail and Frail	1.57 (1.02 - 2.42)	1.54 (0.84 -2.82)
TKI preceding discontinuation			
	Imatinib	Reference	
	Bosutinib/Ponatinib		1.14 (0.37 - 3.53)
	Dasatinib		0.92 (0.43 - 2.00)
	Nilotinib		0.68 (0.30 - 1.55)
NCI comorbidity Index			
	0	Reference	
	≥1	0.80 (0.47 - 1.34)	0.73 (0.37 -1.44)
Number of TKI switches			
	0	Reference	
	1		1.30 (0.70 - 2.40)
	≥2		1.04 (0.45 -2.42)
Time to TKI discontinuation (years)			
			0.72 (0.53 - 0.98)

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