

# Comparable efficacy and safety of generic and branded imatinib for patients with chronic myeloid leukemia in China

Fang Cheng\*, Di Wu\*, Zheng Cui, Qiang Li, Weiming Li and Yu Zhang 

## Abstract

**Background:** Generics imatinib became an alternative treatment option for chronic myeloid leukemia (CML) patients in China. However, clinicians and patients alike harbor concerns regarding the long-term safety of generic imatinib.

**Objectives:** Patients with chronic phase CML receiving frontline imatinib treatment.

**Design:** A retrospective study was used to evaluate the blood concentration, effectiveness, and safety of generic in 170 CML patients.

**Methods:** Imatinib plasma concentrations were detected by high-performance liquid chromatography-tandem mass spectrometry.

**Results:** Among the 170 patients, 73 (42.9%) patients treated with branded imatinib as first-line therapy, while 22 (12.9%) switched to generic imatinib during treatment due to economic considerations. No significant differences in trough concentrations between branded and generic imatinib ( $1549.9 \pm 648.8$  ng/mL vs  $1479.0 \pm 507.0$  ng/mL;  $p=0.95$ ). During the 2-year follow-up, there were no significant differences in molecular response rates (major molecular response (MMR): 33.3% vs 37.0%; deep molecular response: 56.9% vs 42.9%,  $p=0.17$ ) between the branded and generic imatinib. Both groups showed similar rates of switching to second-generation tyrosine kinase inhibitor (11.8% vs 15.1%,  $p=0.56$ ). Furthermore, there were no significant differences in event-free survival or failure-free survival between branded and generic imatinib. Twenty-two (12.9%) switched to generic imatinib during treatment, 68.2% maintained their level of response, 27.3% improved, and only one patient (4.5%) lost MMR. There were no significant differences in the incidence of various adverse events.

**Conclusion:** Generic imatinib are equally effective and safe compared to branded molecules, both for newly diagnosed patients and those who switch from branded.

**Keywords:** blood concentration, chronic myeloid leukemia, efficacy, generic imatinib, safety

Received: 19 February 2024; revised manuscript accepted: 13 June 2024.

## Introduction

The advent of imatinib has significantly revolutionized the management of chronic phase (CP) chronic myeloid leukemia (CML).<sup>1,2</sup> Although tyrosine kinase inhibitors (TKIs) have become the backbone of CML therapy, their exorbitant costs can pose a challenge to patients and health-care systems.<sup>3</sup> In response to the appearance of generics, the reimbursement policies in several

nations have shifted, providing CML patients with an alternative therapeutic choice.<sup>4</sup>

Imatinib remains the primary choice of initial therapy for a large proportion of global CML patients. Since the launch of generic imatinib in 2016, several resource-limited countries, such as China, have incorporated them into their treatment plans. Although researchers anticipated a

*Ther Adv Hematol*

2024, Vol. 15: 1–10

DOI: 10.1177/  
20406207241270806

© The Author(s), 2024.  
Article reuse guidelines:  
[sagepub.com/journals-  
permissions](https://sagepub.com/journals-permissions)

Correspondence to:

**Weiming Li**  
Department of  
Hematology, Union  
Hospital, Tongji Medical  
College, Huazhong  
University of Science  
and Technology, Wuhan  
430022, China  
[lee937@126.com](mailto:lee937@126.com)

**Yu Zhang**

Department of Pharmacy,  
Union Hospital, Tongji  
Medical College, Huazhong  
University of Science  
and Technology, Wuhan  
430022, China

Hubei Key Laboratory of  
Biological Targeted  
Therapy, Union Hospital,  
Tongji Medical College,  
Huazhong University of  
Science and Technology,  
Wuhan 430022, China  
[zhangwkp@163.com](mailto:zhangwkp@163.com)

**Fang Cheng**

Department of Pharmacy,  
Union Hospital, Tongji  
Medical College, Huazhong  
University of Science and  
Technology, Wuhan, China

Hubei Key Laboratory of  
Biological Targeted  
Therapy, Union Hospital,  
Tongji Medical College,  
Huazhong University of  
Science and Technology,  
Wuhan, China

Key Laboratory of  
Hematology, Guangxi  
Medical University,  
Education Department  
of the Guangxi Zhuang  
Autonomous Region,  
Nanning, China

**Di Wu**

Department of  
Hematology, Union  
Hospital, Tongji Medical  
College, Huazhong  
University of Science and  
Technology, Wuhan, China

Zheng Cui  
Qiang Li  
Department of Pharmacy,  
Union Hospital, Tongji  
Medical College, Huazhong  
University of Science and  
Technology, Wuhan, China

Hubei Key Laboratory  
of Biological Targeted  
Therapy, Union Hospital,  
Tongji Medical College,  
Huazhong University of  
Science and Technology,  
Wuhan, China

\*These authors  
contributed equally

substantial outcome similar to the groundbreaking International Randomized Study of Interferon and STI571 (IRIS) trial, actual results can differ due to real-world conditions. Several studies investigating the effectiveness and safety of generically manufactured CML drugs have been published with discrepant outcomes.<sup>5-9</sup> Clinicians and patients alike harbor concerns regarding the long-term safety of generic imatinib. Among the 1518 surveyed CML patients and 259 hematologists,<sup>10</sup> patients expressed their top concerns as TKIs reimbursement policies, TKIs pricing, and new drug development. Conversely, physicians prioritized other issues such as patient monitoring, dose adjustments, and new drug development. While both patients and physicians shared significant apprehension regarding the quality and use of generic drugs, hematologists showed greater concern than patients.

The number of studies evaluating the effectiveness and safety of generic imatinib in CML patients is increasing, although the quantity, particularly in China, remains restricted. This study aimed to evaluate the blood concentration, effectiveness and safety of generic compared with branded imatinib, including newly diagnosed CML-CP patients, and after switching from frontline original imatinib.

## Patients and methods

### Patients

Between January 2019 and December 2022, we retrospectively recruited CML patients received first-line imatinib therapy at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology. Eligibility requirements for participation included a diagnosis of CML-CP treated with first-line imatinib, age over 18 years, and good adherence (good adherence is characterized by timely and correct imatinib intake daily, along with regular attendance of follow-up appointments). Pharmacists conducted compliance assessments every 3–6 months and provided medication education for patients exhibiting sub-optimal compliance levels. Patients were excluded if they had accelerated or blastic phase disease at diagnosis, received first-line treatment with second- (2G) or third-generation TKIs, displayed poor conformity, received medication that could affect imatinib levels, or had incomplete data. We retrospectively collected data on the patients'

clinical information, including demographics, underlying conditions, medication, laboratory results, and adverse events (AEs), through regular outpatient follow-up visits.

### Drug administration

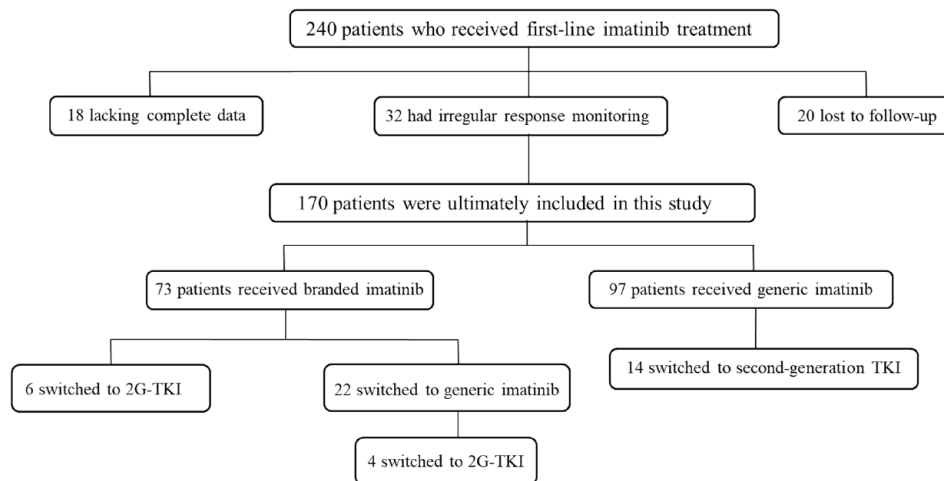
All patients were treated with first-line imatinib, taken once daily at a fixed time, with a standard dose of 400 mg. Dose reduction was implemented in patients with sustained optimal response, in cases of severe AEs, desired a decreased financial burden, or as preparation for discontinuation. Patients with sustained deep molecular response (DMR) for over 2 years could discontinue imatinib with physician guidance based on their medical status. Patients who experienced unacceptable AEs or had treatment failure were switched to second- or third-generation TKIs, such as dasatinib, nilotinib, flumatinib, or olverembatinib.

### Therapeutic drug monitoring

The imatinib trough concentration was achieved after 28 days of uninterrupted treatment and remained stable thereafter. Once this state was reached, blood samples were drawn into EDTA tubes  $24 \pm 2$  h postadministration and centrifuged at  $10,625g$  for 10 min. The plasma was then stored at  $-80^{\circ}\text{C}$  until analysis by high-performance liquid chromatography-tandem mass spectrometry to determine imatinib plasma concentrations.

### Clinical response and outcomes

CML-CP was defined as less than 10% blasts in the peripheral blood or bone marrow, and the absence of extramedullary involvement.<sup>11,12</sup> Therapeutic efficacy assessment based on the 2020 ELN guidelines.<sup>13</sup> Major molecular response (MMR) was specified as a  $BCR::ABL1^{IS}$  level less than 0.1%. The primary objectives were to determine the achievement rate of MMR within 2 years of imatinib treatment and assess the frequency of transitioning to second-generation TKIs. Event-free survival (EFS) refers to the duration from when TKI therapy began until the occurrence of several events, including loss of complete hematological remission (CHR), complete cytogenetic response (CCyR) or major cytogenetic response, loss of MMR, emergence of mutations or clonal chromosome abnormalities in



**Figure 1.** The flow chart of this study.

Ph<sup>+</sup> cells, progression to advanced phase or blast crisis, or death due to any cause. Additionally, failure-free survival (FFS) was calculated from the start date of therapy until treatment discontinuation for any reason except treatment-free remission (TFR), including changing to alternate TKIs.

#### Adverse events

At each follow-up visit, patients carried out hematology and biochemistry analyses. Adverse reactions were recorded in accordance with the Common Terminology Criteria for Adverse Events, version 4.0, and including hematologic AEs such as leukopenia, neutropenia, anemia, and thrombocytopenia; gastrointestinal AEs including nausea, vomiting, and diarrhea, along with other symptoms such as fatigue, periorbital and limb edema, rash, musculoskeletal pain, and conjunctival hemorrhage.

#### Statistical analysis

Descriptive statistics were reported as either percentages or medians with interquartile ranges (IQRs). Categorical variables were compared with the Pearson's chi-squared or Fisher's exact test, whereas continuous variables were evaluated via the Mann-Whitney *U* or Kruskal-Wallis test. Survival probabilities were estimated by means of Kaplan-Meier survival analysis, and these estimates were compared using the log-rank test. Statistical analyses were conducted utilizing IBM

SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA), and statistical significance was observed at the *p* value <0.05 level.

## Results

#### Patient characteristics

The flow chart of our study was shown in Figure 1. Among the 240 patients receiving frontline imatinib treatment, 18 lacking complete data, 32 subjects had irregular response monitoring, and 20 were lost to follow-up were excluded. A total of 170 patients were ultimately included in this study, of whom 86 (50.6%) were male. Among these 170 patients, 73 of them are receiving first-line treatment with branded imatinib (Glivec<sup>®</sup>), while 97 patients are generic imatinib (Xinwei<sup>®</sup>, *n*=57; Genike<sup>®</sup>, *n*=35, and Nuolining<sup>®</sup>, *n*=5). Demographic and clinical data of branded and generic groups are presented in Table 1. Significant differences were observed in the duration of imatinib therapy between the two cohorts. Patients in the branded imatinib group (11.04 years, IQR [7.83–13.52]) had a lengthier median duration of treatment compared to the generic imatinib group (4.76 years, IQR [3.04–6.72], *p*<0.001). Nevertheless, no substantial differences were noted in gender, age, comorbidities, Sokal risk, EUTOS long-term survival score (ELTS score), or TKIs therapy lines between the two cohorts.

In the branded cohort, 22 patients (12.9%) with a median treatment duration of 6.41 years

**Table 1.** Demographic and clinical characteristics between branded and generic groups.

Variables	Branded imatinib (n=73)	Generic imatinib (n=97)	p Value
Sex (male), n (%)	36	50	0.773
Age, years, median (IQR)	53 (43–57)	49 (34–55)	0.073
Duration of therapy, years, median (IQR)	11.04 (7.83–13.52)	4.76 (3.04–6.72)	<0.001
Comorbidity, n (%)			
Hypertension	7 (9.6)	8 (8.2)	0.808
Diabetes	3 (4.1)	5 (5.2)	0.750
Coronary heart disease	3 (4.1)	3 (3.1)	0.722
Hepatitis B	2 (2.7)	7 (7.2)	0.197
Hyperuricemia	11 (15.1)	8 (8.2)	0.120
Hyperlipidemia	5 (6.8)	7 (7.2)	0.926
Gastrointestinal system diseases	7 (9.6)	6 (6.2)	0.408
Other tumors	5 (6.8)	4 (4.1)	0.432
Others	10 (13.7)	10 (10.3)	0.549
Sokal score, n (%)			
Low	21 (28.8)	38 (39.2)	0.956
Intermediate	12 (16.4)	19 (19.6)	
High	5 (6.8)	9 (9.3)	
Unknown	35(47.9)	31(32.0)	
ELTS score, n (%)			
Low	28 (38.4)	49 (50.5)	0.365
Intermediate	5 (6.8)	13 (13.4)	
High	5 (6.8)	4 (4.1)	
Unknown	35 (47.9)	31 (32.0)	
Switch to second-generation TKIs, n (%)	10 (13.7)	14 (14.4)	0.892
TKIs therapy lines, n (%)			
First line	63 (86.3)	83 (85.6)	0.755
Second line	9 (12.3)	11 (11.3)	
Third line	1 (1.4)	3 (3.1)	
Imatinib dose reduction, n (%)			
300 mg	12 (16.4)	17 (17.5)	0.178
200 mg	28 (38.4)	21 (21.6)	

BMI, body mass index; CML, chronic myeloid leukemia; ELTS score, EUTOS long-term survival score; IQR, inter-quartile range; TKI, tyrosine kinase inhibitor.

**Table 2.** Imatinib trough concentrations in branded and generic imatinib.

Imatinib concentration	Branded imatinib (N=44) <sup>a</sup>	Generic imatinib (N=95)	p Value
Imatinib trough concentration <sup>a</sup> (ng/mL)			0.95
Mean ± SD	1549.9 ± 648.8	1479.0 ± 507.0	
Imatinib trough concentration category <sup>b</sup>			0.99
≤1000 ng/mL	7 (15.9)	15 (15.8)	
>1000 ng/mL	37 (84.1)	80 (84.2)	

<sup>a</sup>We measured the imatinib trough concentration of 139 patients who received 400 mg imatinib daily.  
<sup>b</sup>Categorical trough concentration (400 mg daily) are expressed as absolute numbers with the percentage in parenthesis. SD, standard deviation

transitioned to generic imatinib due to economic considerations. Additionally, eight patients exhibited an unfavorable response, while two patients demonstrated intolerance, prompting a switch to 2G-TKIs. In the generic imatinib cohort, 14 (8.2%) patients encountered treatment failure ( $n=11$ ) or intolerance ( $n=3$ ) and subsequently transitioned to a 2G-TKI. Among the 146 patients who did not switch to 2G-TKIs, 78 patients (45.9%) underwent dose reduction (44 prepared for discontinuation, 29 for alleviation of severe AEs, and 5 to mitigate financial burdens), while 10 (5.9%) patients attempted TFR.

#### *Imatinib trough concentration for branded or generic imatinib*

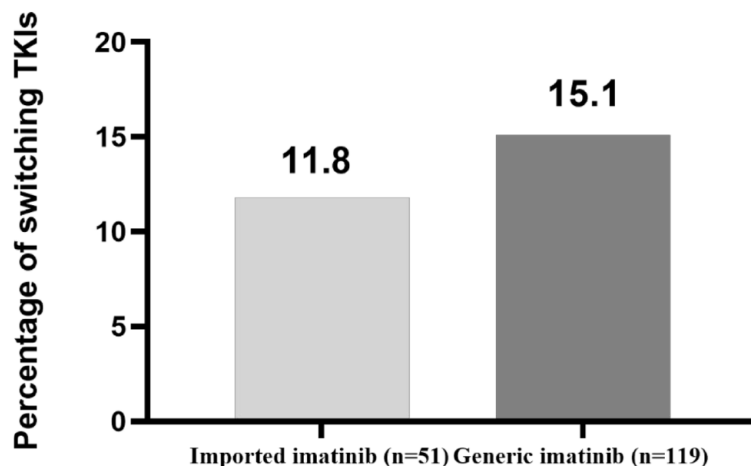
Imatinib trough concentration monitoring requires blood collection within  $24 \pm 2$  h postadministration, coordinated with their medication schedule. Because some patients' medication times do not meet the testing requirements (e.g., if a patient takes medication at 10:00 pm, we are unable to collect their blood for testing), we analyzed the trough concentration of imatinib in 139 patients (branded imatinib,  $n=44$ , generic imatinib,  $n=95$ ) who received a daily dose of 400 mg in this study. The individual trough concentrations of imatinib for branded and generic formulations are presented in Table 2. Our findings revealed no significant differences in trough concentrations between branded and generic forms of imatinib ( $1549.9 \pm 648.8$  ng/mL vs  $1479.0 \pm 507.0$  ng/mL;  $p=0.95$ ) groups. Additionally, we classified the patients receiving 400 mg daily into two categories based on their trough concentration:  $>1000$  and  $\leq 1000$  ng/mL.

The results showed no significant difference in the proportion of patients with trough concentrations  $>1000$  ng/mL between branded and generic imatinib (84.1% vs 84.2%;  $p=0.99$ ).

#### *Relationship between clinical outcomes and branded or generic imatinib*

A total of 24 (14.1%) patients switched to 2G-TKIs, with a median duration of imatinib treatment was 4.70 years (IQR 2.83–9.27 years). The branded or generic imatinib groups showed similar rates of switching to second-generation TKIs (11.8% vs 15.1%,  $p=0.56$ , Figure 2). We also investigate the clinical outcomes of branded or generic imatinib in a sample of 146 patients who did not switch to 2G-TKIs (Table 3). During the 2-year follow-up period, 33.3% and 56.9% of patients in the branded imatinib group achieved MMR and DMR, respectively. In comparison, 37.0% and 42.9% of patients in the generic imatinib group achieved MMR and DMR, respectively. Statistical analysis showed no significant difference in molecular response between the two groups ( $p=0.17$ ). Additionally, 24 (53.3%) and 54 (53.5%) patients underwent reduced imatinib dose in branded and generic imatinib group, respectively ( $p=0.97$ ). Furthermore, there were no significant differences in EFS (84.3% vs 89.1%; hazard ratio (HR), 1.16; 95% CI, 0.49–2.77;  $p=0.73$ , Figure 3(a)) or FFS (74.5% vs 79.0%; HR, 1.15; 95% CI, 0.60–2.22;  $p=0.68$ , Figure 3(b)) between branded and generic imatinib.

Twenty-two patients (12.9%) switched from branded to generic imatinib, and their degree of response after conversion was evaluated



**Figure 2.** Comparison of switching to second-generation tyrosine kinase inhibitor rates between branded and generic imatinib.

**Table 3.** Comparison of clinical outcomes between branded and generic imatinib.

Clinical outcomes	Branded imatinib (N=45) <sup>a</sup>	Generic imatinib (N=101)	p Value
Molecular response <sup>b</sup>			0.17
Non-MMR	2 (9.8)	15 (20.2)	
MMR <sup>c</sup>	16 (33.3)	36 (37.0)	
DMR	27 (56.9)	50 (42.9)	
Low-dose therapy	24 (53.3)	54 (53.5)	0.97
Discontinuation TKIs therapy	3 (6.7)	7 (6.9)	0.97

<sup>a</sup>We investigate the clinical outcomes of branded or generic imatinib in a sample of 146 patients who did not switch to 2G-TKIs.  
<sup>b</sup>We evaluated the molecular response after receiving imatinib treatment for 2 years.  
<sup>c</sup>MMR was defined as  $BCR-ABL1^{IS} \leq 0.1\%$ ; DMR was defined as  $BCR-ABL1^{IS} \leq 0.01\%$ .  
DMR, deep molecular response; MMR, major molecular response; TKI, tyrosine kinase inhibitor.

(Supplemental Table S1). Of these, 68.2% maintained their level of response, 27.3% improved, and only one patient (4.5%) lost MMR. However, four patients underwent a median of 5.41 years of treatment with branded imatinib, then receiving a median of 3.36 years of generic imatinib treatment duo to financial burden. Of these patients, three patients did not achieve MMR, while one patient lost MMR, prompting them to switch to 2G-TKIs.

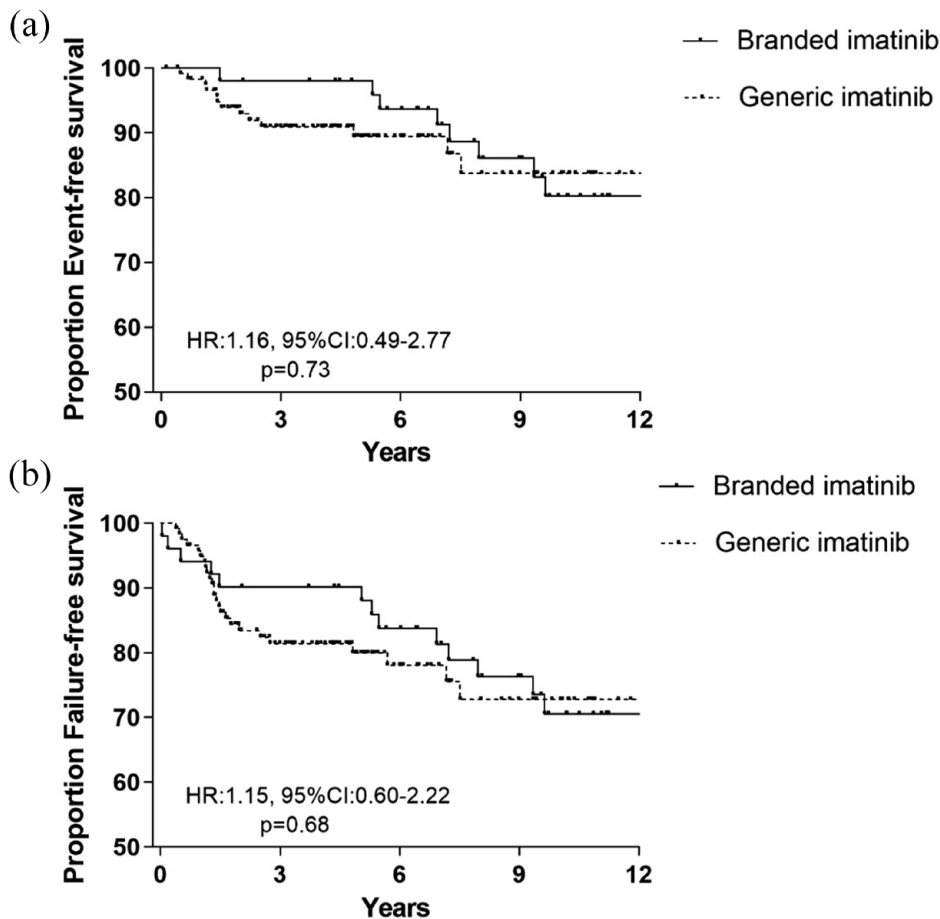
#### *Correlation of branded or generic imatinib with adverse reactions*

Most patients (58.9%) experienced at least one AE while taking branded imatinib, with the most

common being musculoskeletal pain, periorbital and limb edema, anemia, and thrombocytopenia (Table 4). After switching to generic imatinib, six patients reported new or exacerbated AEs, with musculoskeletal pain, fatigue, and hyperuricemia being the most prevalent. Additionally, nine patients maintained low-grade persistent AEs, with severity remaining consistent when transitioning from branded imatinib to generic imatinib.

#### **Discussion**

With the emergence of generic imatinib, reimbursement policies of many countries have been changed, and generics became an alternative



**Figure 3.** The relationship between branded/generic imatinib and clinical outcomes. (a) Event-free survival (EFS); (b) failure-free survival (FFS).

treatment option for CML patients. In this study, we compared the differences between branded and generic imatinib in terms of plasma drug concentration, efficacy, and safety.

Previous research studies have shown a close correlation between imatinib trough concentrations and clinical response in patients with CML.<sup>14-16</sup> Such findings underscore the importance of bioequivalence and bioavailability consistency of generic drugs with the original molecule. In line with this, Natarajan *et al.*<sup>17</sup> evaluated imatinib plasma trough levels in 206 CML-CP patients, where 130 received original imatinib while the remaining 76 were administered two separate generics. The study showed no substantial difference between the plasma trough levels of branded and generic drugs. Similarly, Malhotra *et al.*<sup>18</sup> compared imatinib plasma trough levels among 84 patients taking branded imatinib and 47

receiving generic imatinib. Imatinib plasma trough levels did not differ significantly between both groups. Our results also support previous studies, indicating that generic imatinib has comparable bioavailability to the original molecule.

In newly diagnosed CML-CP patients, Danthala *et al.*<sup>19</sup> conducted a retrospective analysis of 1067 CML-CP patients treated with first-line branded imatinib and 144 patients receiving generics, evaluating both efficacy and safety. Comparable cumulative CCyR rates, EFS, FFS, transformation-free survival (TFS), and overall survival (OS) rates were observed in both groups. No grades 3-4 AEs were reported in either cohorts, although grades 1-2 edema was more prevalent in patients receiving branded imatinib than those given generics (12% vs 5%, respectively). In another study, 442 newly diagnosed CML-CP patients were evaluated (206 patients receiving

**Table 4.** Frequency of AEs associated with treatment using branded and generic imatinib.

Adverse events	Branded imatinib (n = 73)	Generic imatinib persistence AE (severity unchanged from branded imatinib)	Generic imatinib new or worsened AE (severity increased from branded imatinib)
Leukopenia or neutropenia	13 (17.8)	2 (9.1)	1 (4.5)
Anemia	25 (34.2)	3 (13.6)	2 (9.1)
Thrombocytopenia	25 (34.2)	2 (9.1)	1 (4.5)
Diarrhea	18 (24.7)	3 (13.6)	2 (9.1)
Nausea and vomiting	15 (20.5)	2 (19.1)	1 (4.5)
Musculoskeletal pain	29 (39.7)	5 (22.7)	3 (13.6)
Periorbital and limb edema	30 (41.1)	7 (31.8)	2 (9.1)
Rash	13 (17.8)	4 (18.2)	2 (9.1)
Fatigue	5 (6.8)	1 (4.5)	3 (13.6)
Conjunctival hemorrhage	5 (6.8)	1 (4.5)	1 (4.5)
Dyslipidemia	7 (9.6)	2 (9.1)	1 (4.5)
Hyperuricemia	13 (17.8)	2 (9.1)	3 (13.6)
Kidney dysfunction	9 (12.3)	1 (4.5)	1 (4.5)
Overall*	43 (58.9)	9 (40.9)	6 (27.3)

\*This value is not the sum of the column since a patient may have experienced more than one AE.

branded and 236 taking generic imatinib). The cumulative CCyR, MMR, and DMR rates were similar between both groups, and the probability of FFS, progression-free survival, and OS at 4 years did not significantly differ between original molecule and generics. Hematologic and non-hematologic grade >3 AEs were also comparable in both arms.<sup>20</sup>

It is also necessary to investigate the efficacy of patients who first receiving branded imatinib and subsequently switch to generic imatinib treatment. An Italian retrospective study<sup>21</sup> analyzed the sustainability of achieved responses after switching to generic from branded imatinib in 140 CML patients. After a median follow-up period of 19 months postswitch, 84% of patients maintained their responses, while 6% showed improved responses. Molecular fluctuations were detected in 10% of cases, but only one patient lost their response during follow-up. The incidence of AEs worsened in 20% of cases, but only

15% of these AEs were recorded as grade >3. A study was conducted on 200 patients who had been diagnosed with CML-CP.<sup>22</sup> The participants were switched to generic medication after achieving stable CCyR for at least 18 months, following no less than 36 months of imatinib treatment. The results showed that sustained, improved, and worsened molecular response rates under generics were 69%, 25.5%, and 5.5%, respectively. Bonifacio et al.<sup>23</sup> found that switch to generic imatinib for patients who have been receiving branded imatinib for at least six consecutive months appears to be effective and safe.

Several studies have reported comparable efficacy and safety outcomes between CML patients treated with generic and original imatinib. However, some studies have shown contradictory findings regarding their effectiveness and toxicity. Saavedra and Vizcarra<sup>24</sup> analyzed a group of 12 patients who switched from branded imatinib to nonbranded drug, revealing that 5/8 patients



(63%) experienced treatment failure, while 6/8 (75%) suffered severe and recurrent AEs. Furthermore, a prospective study conducted in Iraq found that one-third of 126 CML-CP patients lost CHR after switching to generic imatinib.<sup>7</sup> In contrast, our study showed that generics exhibited similar 2-year MMR rates, EFS, and FFS compared to the original molecule, both in newly diagnosed patients and those who switched medications. Moreover, in terms of safety, no significant differences in toxicities were observed between the original and generics.

Our study has certain limitations. First, it is a single-center retrospective study with a limited number of participants, so further multicenter and large-scale studies are needed to confirm our findings. Second, we did not grade the adverse reactions. In addition, our study did not evaluate the differences between branded/generic imatinib in terms of TFS, OS, adherence, and healthcare costs. Furthermore, there are three generic versions of imatinib available in the Chinese market. However, due to sample size limitations in each group, we did not compare the differences among the three generic imatinib formulations. In conclusion, our results support the notion that generic imatinib are equally effective and safe compared to branded molecules, both for newly diagnosed patients and those who switch from branded imatinib.

## Declarations

### *Ethics approval and consent to participate*

This study has been approved by the institutional ethics committee of Tongji Medical College, Huazhong University of Science and Technology (Wuhan, China) ([2021] 0784) and has been conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all the participants prior to the study.

### *Consent for publication*

All patients and guardians agreed to the publication of this research.

### *Author contributions*

**Fang Cheng:** Data curation; Formal analysis; Funding acquisition; Writing – original draft.

**Di Wu:** Formal analysis; Writing – original draft.

**Zheng Cui:** Data curation; Writing – review & editing.

**Qiang Li:** Formal analysis; Writing – review & editing.

**Weiming Li:** Data curation; Supervision; Writing – review & editing.

**Yu Zhang:** Conceptualization; Writing – review & editing.

### *Acknowledgements*

We would like to thank all participants involved in this study.

### *Funding*

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Open Project of Key Laboratory of Hematology, Guangxi Medical University (GXHKL202305), and the Chinese Pharmaceutical Association Hospital Pharmacy Department (No. CPA-Z05-ZC-2023002).


### *Competing interests*

The authors declare that there is no conflict of interest.

### *Availability of data and materials*

The original contributions presented in the study are included in the article. Further inquiries can be directed to the corresponding authors.

## ORCID iD

Yu Zhang  <https://orcid.org/0000-0003-3630-9002>

## Supplemental material

Supplemental material for this article is available online.

## References

1. Gambacorti-Passerini C and Piazza R. Imatinib—a new tyrosine kinase inhibitor for first-line treatment of chronic myeloid leukemia in 2015. *JAMA Oncol* 2015; 1: 143–144.
2. Stagno F, Stella S, Spitaleri A, et al. Imatinib mesylate in chronic myeloid leukemia: frontline treatment and long-term outcomes. *Expert Rev Anticancer Ther* 2016; 16: 273–278.
3. Dusetzina SB, Winn AN, Abel GA, et al. Cost sharing and adherence to tyrosine kinase

- inhibitors for patients with chronic myeloid leukemia. *J Clin Oncol* 2014; 32: 306–311.
4. Padula WV, Larson RA, Dusetzina SB, et al. Cost-effectiveness of tyrosine kinase inhibitor treatment strategies for chronic myeloid leukemia in chronic phase after generic entry of imatinib in the United States. *J Natl Cancer Inst* 2016; 108: djw003.
  5. de Lemos ML and Kyritsis V. Clinical efficacy of generic imatinib. *J Oncol Pharm Pract* 2015; 21: 76–79.
  6. Pagnano KB, Fava C, Miranda EC, et al. Efficacy and safety of generic imatinib compared to glivec in chronic phase – chronic myeloid leukemia – a multicenter, observational study. *Blood* 2018; 132: 46.
  7. Alwan AF, Matti BF, Naji AS, et al. Prospective single-center study of chronic myeloid leukemia in chronic phase: switching from branded imatinib to a copy drug and back. *Leuk Lymphoma* 2014; 55: 2830–2834.
  8. Eskazan AE, Ayer M, Kantarcioglu B, et al. First line treatment of chronic phase chronic myeloid leukaemia patients with the generic formulations of imatinib mesylate. *Br J Haematol* 2014; 167: 139–141.
  9. Eskazan AE and Soysal T. The tolerability issue of generic imatinib in patients with chronic myeloid leukemia (*Comment on Adi J. Klil-Drori et al., Haematologica* 2019;104(7):e293). *Haematologica* 2019; 104: e330.
  10. Jiang Q, Yu L and Gale RP. Patients' and hematologists' concerns regarding tyrosine kinase-inhibitor therapy in chronic myeloid leukemia. *J Cancer Res Clin Oncol* 2018; 144: 735–741.
  11. Baccarani M, Saglio G, Goldman J, et al. Evolving concepts in the management of chronic myeloid leukemia: recommendations from an expert panel on behalf of the European LeukemiaNet. *Blood* 2006; 108: 1809–1820.
  12. Baccarani M, Cortes J, Pane F, et al. Chronic myeloid leukemia: an update of concepts and management recommendations of European LeukemiaNet. *J Clin Oncol* 2009; 27: 6041–6051.
  13. Hochhaus A, Baccarani M, Silver RT, et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. *Leukemia* 2020; 34: 966–984.
  14. Cheng F, Zeng F, Li Q, et al. Imatinib dose optimization based on therapeutic drug monitoring in Chinese patients with chronic-phase chronic myeloid leukemia. *Cancer* 2022; 128: 3951–3958.
  15. Clarke WA, Chatelut E, Fotoohi AK, et al. Therapeutic drug monitoring in oncology: International Association of Therapeutic Drug Monitoring and Clinical Toxicology consensus guidelines for imatinib therapy. *Eur J Cancer* 2021; 157: 428–440.
  16. Cortes JE, Egorin MJ, Guilhot F, et al. Pharmacokinetic/pharmacodynamic correlation and blood-level testing in imatinib therapy for chronic myeloid leukemia. *Leukemia* 2009; 23: 1537–1544.
  17. Natarajan H, Kumar L, Bakhshi S, et al. Imatinib trough levels: a potential biomarker to predict cytogenetic and molecular response in newly diagnosed patients with chronic myeloid leukemia. *Leuk Lymphoma* 2019; 60: 418–425.
  18. Malhotra H, Sharma P, Bhargava S, et al. Correlation of plasma trough levels of imatinib with molecular response in patients with chronic myeloid leukemia. *Leuk Lymphoma* 2014; 55: 2614–2619.
  19. Danthala M, Gundeti S, Kuruva SP, et al. Generic imatinib in chronic myeloid leukemia: survival of the cheapest. *Clin Lymphoma Myeloma Leuk* 2017; 17: 457–462.
  20. Dou X, Qin Y, Lai Y, et al. Comparable efficacy and safety of generic imatinib and branded imatinib in patients with newly diagnosed chronic myeloid leukemia with a consideration of socioeconomic characteristics: a retrospective study from a single center. *Clin Lymphoma Myeloma Leuk* 2020; 20: e304–e315.
  21. Scalzulli E, Colafigli G, Latagliata R, et al. Switch from branded to generic imatinib: impact on molecular responses and safety in chronic-phase chronic myeloid leukemia patients. *Ann Hematol* 2020; 99: 2773–2777.
  22. Gemelli M, Elli EM, Elena C, et al. Use of generic imatinib as first-line treatment in patients with chronic myeloid leukemia (CML): the GIMS (Glivec to Imatinib Switch) study. *Blood Res* 2020; 55: 139–145.
  23. Bonifacio M, Scaffidi L, Binotto G, et al. Safety and efficacy of switching from branded to generic imatinib in chronic phase chronic myeloid leukemia patients treated in Italy. *Leuk Res* 2018; 74: 75–79.
  24. Saavedra D and Vizcarra F. Deleterious effects of non-branded versions of imatinib used for the treatment of patients with chronic myeloid leukemia in chronic phase: a case series on an escalating issue impacting patient safety. *Leuk Lymphoma* 2014; 55: 2813–2816.