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Use of tyrosine kinase inhibitor dispensing records as an indicator of non-adherence to chronic myeloid leukemia treatment

Priscilla Joplin CIODARO[1,4], Milene Rangel DA COSTA[2], Thiago Botelho AZEREDO[3,4]

[1]Instituto Estadual de Hematologia Arthur de Siqueira Cavalcanti, Rio de Janeiro, Brasil; [2]Departamento de Fármacos e Medicamentos, Faculdade de Farmácia, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, Brasil; [3]Observatório de Vigilância e Uso de Medicamentos, Faculdade de Farmácia, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, Brasil; [4]Programa de Pós-Graduação em Ciência e Tecnologia Farmacêutica (CTECFAR), Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, Brasil.

Corresponding author: Ciodaro PJ, priscillajoplin@gmail.com

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Abstract

Objective: The present study aimed to analyze the regularity of tyrosine kinase inhibitors (TKI) dispensing and the factors associated with chronic myeloid leukemia (CML) treatment in a hematology reference center in the state of Rio de Janeiro, Brazil. **Methods:** This observational, descriptive, cross-sectional and retrospective study analyzed drug dispensing data from the pharmacy for 173 patients using dasatinib or nilotinib for at least six months, as well as those who were on imatinib but switched to another line of therapy during the study period, from 2019 to 2022. Sociodemographic and treatment-related data were collected from electronic medical records in the institution's system. **Results:** Considering adherence as medication possession greater than 90%, adherence in 2019 was 74%, decreasing in 2020 and 2021, and rising again in 2022 to 66%. It is discussed that the negative impact of the COVID-19 pandemic on adherence was offset by administrative measures that expanded medication possession. Through bivariate analyses, it was observed that men and individuals living closer to the dispensing unit were twice as likely to be adherent. **Conclusion:** The use of medication registry data to apply this and other indicators of persistence and adherence in chronic diseases, including CML, has been widely adopted and may serve as a facilitator in this process.

Keywords: chronic myeloid leukemia, tyrosine kinase inhibitors, medication adherence, service indicators.

Utilização de registros de dispensação de inibidores de tirosina quinase como indicador de não adesão ao tratamento da leucemia mieloide crônica

Resumo

Objetivo: O presente estudo teve como objetivo analisar a regularidade das dispensações de inibidores de tirosina quinases (ITQ) e os fatores associados ao tratamento da leucemia mieloide crônica (LMC) em um centro de referência em hematologia no estado do Rio de Janeiro, Brasil. **Métodos:** Este estudo observacional, descritivo, transversal e retrospectivo analisou dados de dispensação de medicamentos na farmácia de 173 pacientes em uso de dasatinibe ou nilotinibe por pelo menos seis meses, bem como daqueles que estavam em tratamento com imatinibe, mas mudaram para outra linha terapêutica durante o período do estudo, de 2019 a 2022. Dados sociodemográficos e relacionados ao tratamento foram coletados a partir dos prontuários eletrônicos do sistema da instituição. **Resultados:** Considerando adesão como posse de medicamento superior a 90%, a adesão foi de 74% em 2019, diminuiu em 2020 e 2021 e voltou a subir em 2022, atingindo 66%. Discute-se que o impacto negativo da pandemia de COVID-19 sobre a adesão foi compensado por medidas administrativas que ampliaram a posse de medicamentos. Por meio de análises bivariadas, observou-se que homens e indivíduos que residiam mais próximos à unidade dispensadora apresentaram o dobro de chances de adesão. **Conclusão:** O uso de dados de registros de medicamentos para aplicação deste e de outros indicadores de persistência e adesão em doenças crônicas, incluindo a LMC, vem sendo amplamente adotado e pode atuar como facilitador nesse processo.

Palavras-chave: leucemia mieloide crônica, inibidores de tirosina quinase, adesão à medicação, indicadores de serviços.

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Introduction

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm[1] characterized by the presence of the Philadelphia chromosome (Ph+), resulting from a reciprocal translocation between the long arms of chromosomes 9q34 and 22q11. This genetic alteration leads to the formation of the BCR-ABL fusion oncoprotein, which exhibits abnormally increased tyrosine kinase activity.[2] According to the Clinical Protocol and Therapeutic Guidelines for CML (PCDT) issued by the Ministry of Health (Ministério da Saúde) (2021), the recommended treatment in Brazil, provided through the public health system, consists of the use of tyrosine kinase inhibitors (TKIs) — imatinib, dasatinib, and nilotinib.

Medication adherence can be divided into three phases: initiation, implementation, and discontinuation. *Initiation* refers to the first prescribed dose taken by the patient; *implementation* concerns the extent to which the patient's actual dosing corresponds to the prescribed regimen, from the first to the last dose; and *discontinuation* marks the end of pharmacotherapy, when the last dose is omitted and no further doses are taken. The term persistence is used to describe the period between treatment initiation and its end with the final dose, preceding discontinuation.[3]

Patients with CML may experience difficulties adhering to pharmacotherapy due to adverse events associated with TKI treatment.[4] To evaluate adherence to any prescribed therapy, assessment methods classified as direct or indirect are employed; however, there is no established gold standard.[5] Pharmacy refill records (dispensing records) constitute an indirect, low-cost method, as they are derived from computerized dispensing systems through review of patient charts and medication histories.[6] Institutional secondary databases can provide valuable information on these records, which are used to construct indicators for adherence assessment.[7]

The most commonly used indicators to measure adherence in chronic diseases are the medication possession ratio (MPR) and the proportion of days covered (PDC).[8] The PDC has been widely used to assess adherence and as a persistence indicator. It calculates the number of days the patient has medication available, typically expressed as a percentage, and does not allow values above 100%, as these would indicate over-dispensing.[7,8] These records provide indicators that may enable identification of patients who have difficulty obtaining their medication and, beyond that, those with limitations in maintaining therapy.[7]

Therefore, the present study aimed to estimate adherence and its associated factors in the treatment of CML by analyzing the regularity of TKI refills at a tertiary care unit specialized in hematologic diseases in the city of Rio de Janeiro.

Methods

This observational, descriptive, cross-sectional, and retrospective study was conducted at a hematology referral institute in the state of Rio de Janeiro. Patients aged 18 years or older who were followed at the institution between January 1, 2019, and December 31, 2022 were included, provided they had been receiving treatment for at least six months at the start of the study with a tyrosine kinase inhibitor (TKI) — dasatinib or nilotinib (as second- or third-line therapy). Patients who were on first-line therapy (imatinib) in January 2019 and subsequently switched to second- or third-line therapy during the follow-up period were also included. Exclusion criteria comprised patients with CML who initiated treatment at any time during the study period, those transferred to other institutions for follow-up, and those who remained on first-line therapy throughout the entire study period.

Data collection was performed using the institution's computerized administrative system, which stores patient information in electronic medical records and manages inventory control. Patient profile characterization was carried out through analysis of the variables sex, age, marital status, race, and education level. The postal code variable was used to calculate the distance between the patient's residence and the treatment unit using the Global Positioning System (GPS). Dates of death were obtained from electronic medical records and from the website of the Court of Justice of Rio de Janeiro (Tribunal de Justiça do Rio de Janeiro – TJRJ), through the birth and death records query, to determine the study mortality rate.

Treatment characteristics — including the TKIs used and the line of therapy — were collected individually to characterize patients' pharmacological treatment profiles. Dispensing records of TKI medications, including refill dates and quantities dispensed, were extracted from monthly managerial reports for each formulation over the four-year period. These data enabled identification of a proxy variable for the adherence outcome, calculated using the proportion of days covered (PDC) indicator.

A descriptive analysis using frequency distributions of sociodemographic and treatment-related variables was performed. Sociodemographic variables were categorized as follows: sex (female, male); age group (older adults — > 60 years; non-older adults — others); marital status (with partner, without partner); race (White, Black, and Brown); education (incomplete primary education; complete primary education or higher); and distance from residence (> 45 km (approximately 28 miles) vs < 45 km from the institution). The 45-km cutoff was defined after analyzing the distribution of distances observed.

Medication availability during the observation period was assessed using dispensing records through calculation of PDC for each patient in each study year:

$$\text{PDC} = \frac{\text{Number of days the patient had the medication available X 100}}{\text{Observation period (days)}}$$

In the descriptive analysis of persistence, the mean PDC was calculated. For bivariate analyses, the variable was categorized into two groups using a 90% PDC cutoff[9], with patients classified as "adherent" when PDC ≥ 90%. Bivariate analyses were performed comparing PDC results with the sociodemographic characteristics of the study population. Differences in proportions were assessed using the chi-square test, with a significance level of 0.05. The magnitude of association was estimated using the odds ratio (OR) with a 95% confidence interval (95% CI).

All collected variables were entered into Microsoft Excel spreadsheets, and statistical analyses were subsequently conducted using SPSS software version 22.0.

This study was designed in accordance with the Brazilian Guidelines and Regulatory Standards for Research Involving Human Subjects (Resolution 466/2012). It was submitted to the Institutional Research Ethics Committee (CAAE: 68127223.2.0000.5267), and the requirement for written informed consent was waived.

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Results

The sociodemographic characteristics of the 173 selected patients are presented in Table 1. The distribution by sex showed a slight predominance of men, representing 57.2% of the study population. Patients aged 60 years and older comprised the majority (54.9%). Regarding education level, 43.9% had not completed primary education (fewer than nine years of schooling). Among the 64.2% who lived within 45 km of the treatment center, 78 patients resided in the city of Rio de Janeiro. Concerning race/ethnicity, 51.5% self-identified as White, representing the largest group. Over the four-year study period, 33 patients died, of whom 63.0% (21) were male and 81.0% (27) were older than 60 years. It was not possible to infer causality for deaths in this analysis.

Regarding lines of therapy, most patients were receiving second-line treatment. In 2019, of 115 patients, 81 (70.4%) were treated with dasatinib; in 2020, 72 of 103 patients (70.0%) used this medication; in 2021, 67 patients (65.0%); and in 2022, 65 patients (63.7%) remained on dasatinib. For nilotinib, the numbers were lower: 34 patients in 2019, 31 in 2020, 36 in 2021, and 37 in 2022. For third-line therapy, there was a decrease over time, with nilotinib as the most prevalent drug: 25 of 40 patients in 2019, 23 of 34 in 2020, 23 of 32 in 2021, and 21 of 27 in 2022. Regarding imatinib, 17 patients were using the drug in 2019 (two in third-line), 14 in 2020 (two in third-line), and five in 2021. In 2022, no patients were receiving imatinib. Acquisition of imatinib for third-line patients was funded by the institution's own resources, in accordance with the Clinical Protocol and Therapeutic Guidelines (PCDT).

Table 1. Description of the sociodemographic characteristics of the study population

Variables	N	Percentage (%)
Sex		
Female	74	42.8
Male	99	57.2
Age group		
< 60 years	78	45.1
≥ 60 years	95	54.9
Education level		
Incomplete primary education	76	43.9
Complete primary education or higher	97	56.1
Marital status		
With partner	92	53.2
Without partner	81	46.8
Distance from residence > 45 km		
No	112	64.8
Yes	61	35.2
Race/ethnicity		
White	89	51.5
Brown	64	37.0
Black	20	11.5
Total	173	100

Adherence and persistence analyses were performed separately for each year of the study period, including 171 patients in 2019, 150 in 2020, 140 in 2021, and 129 in 2022. The variation in the number of patients across years was due to the absence of dispensing records for the entire year in some cases, resulting from death or treatment discontinuation. Using medication refill data, it was possible to calculate the PDC for each patient across the four study years, determining the mean medication possession. The mean possession (mean PDC) was 90.0% in 2019, decreasing slightly in 2020 and 2021 (86.0%), and increasing again in 2022 (88.0%). Considering adherence to tyrosine kinase inhibitors in this study as medication possession above 90% (PDC > 90%), 74% of patients were adherent in 2019, decreasing to 54.0% in 2020 and 51.0% in 2021, and increasing again in 2022, when 66.0% of patients were classified as adherent.

Through bivariate analyses, sociodemographic characteristics — age, sex, marital status, education, race/ethnicity, and distance from residence to the institution — were compared with adherence (Table 2). Over the entire study period, 92 patients were classified as adherent (PDC > 90%). The proportion of adherent patients was higher among older adults (58.9%), although this result was not statistically significant. There was a statistically significant association between sex and adherence (p = 0.024), with a higher proportion of adherence among male patients (approximately twofold higher odds of adherence among men). No association was found between adherence and marital status, education level, or race/ethnicity. Among patients living within 45 km of the institution, 60% were adherent, whereas among those living farther away, the proportion was below 40.0% (p = 0.007). The analyses confirmed that patients residing within 45 km of the hospital had 2.4 times higher odds of adherence.

Table 2. Association between sociodemographic variables and adherence (possession >90%, according to PDC)

Category	Adherence N	Percentage (%)	p-Value	Odds Ratio OR (95% CI)
Age group				
< 60 years	36	46.2	0.93	1.675 [0.91-3.06]
>= 60 years	56	58.9		
Sex				
Female	32	43.2	0.024	0.495 [0.26-0.91]
Male	60	60.6		
Marital status				
With partner	49	53.2	0.982	1.007 [0.55-1.83]
Without partner	42	51.8		
Education level				
Incomplete primary education	35	46.1	0.175	1.518 [0.83-2.77]
Complete primary education or higher	56	57.7		
Distance from residence to dispensing unit				
< 45 km	68	60.7	0.007	0.420 [0.22-0.79]
>= 45 km	24	39.3		
Race/ethnicity				
White	50	56.2	0.416	1.282 [0.70-2.33]
Non-white	42	50.0		

Legend: N = number of patients; p-Value with significance level of 0.05; OR = odds ratio; 95% CI = 95% confidence interval.

Discussion

An observational study conducted in 27 European countries provided extensive information on the clinical and demographic characteristics of patients with CML, demonstrating that the incidence of the disease increases with age and is higher in men than in women.[10]

Another study conducted in Sweden between 2002 and 2010, including 779 individuals diagnosed with CML with a median age of 60 years, reported a ratio of 1.2 men for every woman.[11] Data from the National Cancer Institute (2024) in the United States also showed a prevalence ratio of 1.3 men for every woman with CML across all ages, and 1.2 among patients older than 65 years (data as of January 2021). In the present study, this pattern was confirmed, with male patients representing 57.2% of the population, corresponding to a ratio of 1.3 men for every affected woman.

According to the National Comprehensive Cancer Network (NCCN), the median age at disease onset is 67 years.[12] In developing countries, where the population tends to be younger, the average age at diagnosis and incidence may be lower compared with developed countries[13]. In this study, age group categorization showed a higher prevalence of the disease among patients older than 60 years (54.9%), with 28.3% in the 60–69-year age group.

Following the introduction of second-generation tyrosine kinase inhibitors (TKIs), overall survival among older patients with CML has improved significantly. A retrospective study conducted in Italy including 2,315 patients in the chronic phase of the disease showed that the mortality rate in the 60–74-year age group, compared with the general population, was below 1%.[14] In the present study, analysis of deaths indicated that the majority occurred among patients older than 65 years, representing 66.6% of the 33 deaths recorded between 2019 and 2022.

In addition to prevalence data, studies suggest that men have higher mortality rates in CML than women. Biological factors, comorbidities, and genetic factors — including a higher prevalence of high-risk gene mutations among males — as well as treatment-related factors, may contribute to a greater likelihood of disease progression to acute leukemia, resulting in longer survival among women.[14] Findings in this study are consistent with this pattern: 21 men died, representing 63.3% of total deaths.

A study conducted in the United States with epidemiological data from 1992 to 2001 showed that incidence varies across ethnic groups, being 1.42 times higher in non-Hispanic White older adults than in Hispanics, and 1.22 times higher than in Black individuals.[15] Another U.S. study reported that between 1997 and 2002, CML incidence was higher among non-Hispanic Whites compared with other ethnic groups.[16] In the present study, patients who self-identified as White accounted for 51.5% of the sample. Compared with the total population, this corresponds to a ratio of 1.05 White to non-White patients, a less pronounced difference than that reported in the cited studies.

Regarding medication use across treatment lines, dasatinib was the most frequently used drug in second-line therapy. A comparative Italian study published in 2021 found that 55% of CML patients received dasatinib as second-line therapy, compared with 45% receiving nilotinib.[17] Considering the most common adverse events associated with each drug — pleural effusion and hematologic adverse events for dasatinib, and cardiovascular effects for nilotinib[12,17] — the predominance of dasatinib in second-line therapy in this study may be related to dosing convenience and patient comorbidities.

There is no specific institutional protocol; the institution follows recommendations from the Clinical Protocol and Therapeutic Guidelines (PCDT) issued by the Ministry of Health (Ministério da Saúde). However, some clinical decisions documented in medical records indicate that first-line agents according to the national protocol have been used as third-line options in the studied unit. The absence of a clearly defined third-line recommendation in the PCDT and the lack of a specific institutional protocol may explain individualized clinical decisions aimed at maintaining therapy.

In adherence research, the scarcity of detailed clinical records often limits validation of information. Consequently, many studies rely on secondary databases to analyze data and develop indicators for assessing adherence and its determinants.[7] One commonly used indicator in chronic diseases is the proportion of days covered (PDC). Evidence from the literature suggests that this indicator can identify potentially non-adherent patients; however, it cannot ensure that non-adherence is solely due to lack of medication possession, as clinical and behavioral factors may also play a role.[18]

There was a 27–31% reduction in the proportion of patients classified as adherent in 2020 and 2021 compared with the first year analyzed. This decline coincided with the COVID-19 pandemic period. The need for quarantine and social distancing, combined with patients' fear of infection, may have contributed to reduced or delayed attendance at the institution for TKI refills. Several studies have shown that medication adherence was affected during the pandemic. According to a systematic review, many chronic treatments experienced reduced adherence or were interrupted during this period, with contributing factors including fear of infection, limited access to healthcare professionals, and medication shortages.[19] On the other hand, although a considerable proportion of patients experienced reduced adherence during this period (approximately 20–23%), the mean medication possession decreased by only 4%. This suggests that the decline in adherence might have been more severe had dispensing protocols not been adapted to provide larger medication supplies, reducing the need for frequent visits to the institution.

Some studies indicate that younger and single patients are more likely to have lower adherence, and that this age group may also be more prone to future treatment interruptions due to costs and adverse reactions.[20] Older patients may also experience compromised adherence because of additional challenges, such as lower tolerance to TKI adverse effects, comorbidities, polypharmacy, and socioeconomic issues.[21] The complexity of dosing regimens, combined with forgetfulness, limited understanding, reduced visual acuity, and decreased manual dexterity, contributes to medication administration errors among older adults, acting as barriers to adherence[22].

In this study, adherence was higher among men. A multicenter study involving 63 countries evaluated factors influencing adherence in CML and, although no causal relationship with sex was established, male sex was associated with higher adherence ($p = 0.0002$).[23] A Polish study including 140 patients receiving imatinib, dasatinib, or nilotinib assessed adherence through a questionnaire and found no statistically significant difference between sexes ($p = 0.237$).[24] When applying the PDC indicator, a retrospective cohort study found that men treated with imatinib had higher adherence than women (PDC > 90%), although the difference was not statistically significant ($p = 0.37$).[9]

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Journal of Hospital Pharmacy and Health Services

Lower adherence among women may be related to adverse effects. A study evaluating adherence to imatinib found that women more frequently reported negative impacts of adverse effects on quality of life, which may lead to interruptions, irregular use, or lower persistence[25].

Research has highlighted that a greater ability to access, understand, and use medication information safely and effectively is directly associated with higher education levels.[26] In this study, a higher proportion of adherent patients was observed among those with higher education; however, this finding was not statistically significant.

Regarding distance, patients living within 45 km of the institution had twice the odds of adherence. The World Health Organization states that in developing countries, transportation costs and distance from healthcare centers can negatively affect adherence[27]. Greater geographic distance from treatment centers creates logistical and financial barriers, such as increased travel time and costs, loss of workdays, and difficulty accessing consultations and medications. This may reduce adherence and limit patient contact with healthcare teams, thereby restricting clinical monitoring and adverse event management.[28,29]

The analyses also showed a higher proportion of adherence among patients who self-identified as White (without statistical significance). Some studies report higher adherence among White patients[30], while others indicate that Black patients report greater difficulties in taking CML medications compared with White patients.[31]

The main study limitations relate to deficiencies in the institution's electronic medical records, including absence of RQ-PCR test results performed outside the institution, incomplete information on disease phase, reasons for dose reduction or therapy change, and data on treatment start date and duration. If available, these variables could have strengthened the analyses and enabled a more precise evaluation of the relationship between specific treatment lines or medications and adherence.

Conclusion

Treatment of chronic myeloid leukemia (CML) has advanced substantially with the advent of tyrosine kinase inhibitors (TKIs), transforming it from a high-mortality disease into a chronic condition requiring long-term therapy, thereby improving patients' quality of life. Ensuring continuity of medication use is therefore essential.

Medication adherence in CML presents several challenges. In this study, using the proportion of days covered (PDC) indicator, it was possible to verify that certain sociodemographic variables directly influenced adherence, particularly sex and distance from residence to the treatment center. Variables such as age, education level, race/ethnicity, and marital status did not show statistically significant associations. Additionally, the COVID-19 pandemic negatively affected patients' medication-seeking behavior and, consequently, medication possession, although logistical adjustments may have mitigated this impact.

The use of medication dispensing records to generate indicators of persistence and adherence in chronic diseases, including CML, has been widely adopted and can facilitate monitoring. However, incomplete or inadequate treatment documentation remains a critical limitation, restricting the scope and robustness of such studies.

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Collaborators

CIODARO PJ contributed to the conceptualization, study design, planning, literature review, analysis and interpretation of results, manuscript drafting, and approval of the final version. AZEREDO TB contributed to the conceptualization, study design, planning, analysis and interpretation of results, manuscript drafting, and approval of the final version. COSTA MR contributed to the analysis and interpretation of results.

Conflict of Interests

The authors declare no conflicts of interest related to this article.

References

1. Rowley JD. Letter: A new consistent chromosomal abnormality in chronic myelogenous leukaemia identified by quinacrine fluorescence and Giemsa staining. Nature. 1973;243(5405):290-293. doi:10.1038/243290a0
2. Frazer R, Irvine AE, McMullin MF. Chronic myeloid leukaemia in the 21st century. *Ulster Med J.* 2007;76(1):8-17. doi: 10.3109/10428199309047855
3. Vrijens B, De Geest S, Hughes DA, et al. A new taxonomy for describing and defining adherence to medications. Br J Clin Pharmacol. 2012;73(5):691-705. doi:10.1111/j.1365-2125.2012.04167.x
4. Efficace F, Cottone F, Yanez B, et al. Patient-reported symptom monitoring and adherence to therapy in patients with newly diagnosed chronic myeloid leukemia. Cancer. 2024;130(2):287-299. doi:10.1002/cncr.35021
5. Leite SN, Vasconcellos MPC. Adesão à terapêutica medicamentosa: elementos para a discussão de conceitos e pressupostos adotados na literatura. *Cien Saude Colet.* 2003;8(3):775-782. doi:10.1590/S1413-81232003000300011
6. Obreli-Neto PR, Prado MF, Vieira JC, et al. Métodos de avaliação de adesão à farmacoterapia. Rev Bras Farm. 2012;93:403-410. doi:10.14450/2318-9312.v26.e1.a2014.pp11-26

7. Lima-Dellamora EC, Osorio-de-Castro CGS, Madruga LGSL, et al. Utilização de registros de dispensação de medicamentos na mensuração da adesão: revisão crítica da literatura. *Cad Saude Publica.* 2017;33(3):e00136216. doi:10.1590/0102-311X00136216

8. Peterson AM, Nau DP, Cramer JA, et al. A checklist for medication compliance and persistence studies using retrospective databases. Value Health. 2007;10(1):3-12. doi:10.1111/j.1524-4733.2006.00139.x

9. Michiels S, Tricas-Sauras S, Salaroli A, et al. Imatinib Adherence and Persistence in Patients with Chronic Myeloid Leukemia in Belgium: Evidence from Real-World Data. Patient Prefer Adherence. 2024;18:1991-2006. doi:10.2147/PPA.S472478

10. Hoffmann VS, Baccarani M, Hasford J, et al. The EUTOS population-based registry: incidence and clinical characteristics of 2904 CML patients in 20 European Countries. Leukemia. 2015;29(6):1336-1343. doi:10.1038/leu.2015.73

11. Höglund M, Sandin F, Hellström K, et al. Tyrosine kinase inhibitor usage, treatment outcome, and prognostic scores in CML: report from the population-based Swedish CML registry. Blood. 2013;122(7):1284-1292. doi:10.1182/blood-2013-04-495598

12. Shah NP, Bhatia R, Altman JK, et al. Chronic Myeloid Leukemia, Version 2.2024, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2024;22(1):43-69. doi:10.6004/jnccn.2024.0007

13. Mendizabal AM, Younes N, Levine PH. Geographic and income variations in age at diagnosis and incidence of chronic myeloid leukemia. Int J Hematol. 2016;103(1):70-78. doi:10.1007/s12185-015-1893-y

14. Breccia M, Celant S, Olimpieri PP, et al. Mortality rate in patients with chronic myeloid leukemia in chronic phase treated with frontline second-generation tyrosine kinase inhibitors: a retrospective analysis by the monitoring registries of the Italian Medicines Agency (AIFA). Ann Hematol. 2021;100(2):481-485. doi:10.1007/s00277-021-04406-1

15. Matasar MJ, Ritchie EK, Consedine N, et al. Incidence rates of the major leukemia subtypes among US Hispanics, Blacks, and non-Hispanic Whites. Leuk Lymphoma. 2006;47(11):2365-2370. doi:10.1080/10428190600799888

16. Yamamoto JF, Goodman MT. Patterns of leukemia incidence in the United States by subtype and demographic characteristics, 1997-2002. Cancer Causes Control. 2008;19(4):379-390. doi:10.1007/s10552-007-9097-2

17. Scalzulli E, Caocci G, Efficace F, et al. Real-life comparison of nilotinib versus dasatinib as second-line therapy in chronic phase chronic myeloid leukemia patients. Ann Hematol. 2021;100(5):1213-1219. doi:10.1007/s00277-021-04477-0

18. de Oliveira Costa J, Zhao Y, Pearson SA, Schaffer AL. Assessing the impact of implementing multiple adherence measures to antiretroviral therapy from dispensing data: a short report. AIDS Care. 2023;35(7):970-975. doi:10.1080/09540121.2022.2050179

19. Olmastroni E, Galimberti F, Tragni E, et al. Impact of COVID-19 Pandemic on Adherence to Chronic Therapies: A Systematic Review. Int J Environ Res Public Health. 2023;20(5):3825. doi:10.3390/ijerph20053825

20. Jiang Q, Liu ZC, Zhang SX, et al. Young age and high cost are associated with future preference for stopping tyrosine kinase inhibitor therapy in Chinese with chronic myeloid leukemia. J Cancer Res Clin Oncol. 2016;142(7):1539-1547. doi:10.1007/s00432-016-2159-7

21. Russo D, Malagola M, Skert C, et al. Treatment of chronic myeloid leukemia elderly patients in the tyrosine kinase inhibitor era. Curr Cancer Drug Targets. 2013;13(7):755-767. doi:10.2174/15680096113139990090

22. Wimmer BC, Cross AJ, Jokanovic N, et al. Clinical Outcomes Associated with Medication Regimen Complexity in Older People: A Systematic Review. J Am Geriatr Soc. 2017;65(4):747-753. doi:10.1111/jgs.14682

23. Geissler J, Sharf G, Bombaci F, et al. Factors influencing adherence in CML and ways to improvement: Results of a patient-driven survey of 2546 patients in 63 countries. J Cancer Res Clin Oncol. 2017;143(7):1167-1176. doi:10.1007/s00432-017-2372-z

24. Rychter A, Jerzmanowski P, Hołub A, et al. Treatment adherence in chronic myeloid leukaemia patients receiving tyrosine kinase inhibitors. Med Oncol. 2017;34(6):104. doi:10.1007/s12032-017-0958-6

25. Efficace F, Baccarani M, Breccia M, et al. Health-related quality of life in chronic myeloid leukemia patients receiving long-term therapy with imatinib compared with the general population. *Blood*. 2011;118(17):4554-4560. doi:10.1182/blood-2011-04-347575

26. Plaza-Zamora J, Legaz I, Osuna E, et al. Age and education as factors associated with medication literacy: a community pharmacy perspective. *BMC Geriatr*. 2020;20(1):501. doi:10.1186/s12877-020-01881-5

27. World Health Organization. Adherence to Long-Term Therapies: Evidence for Action. Geneva: WHO; 2003.

28. Ambroggi M, Biasini C, Del Giovane C, et al. Distance as a Barrier to Cancer Diagnosis and Treatment: Review of the Literature. Oncologist. 2015;20(12):1378-1385. doi:10.1634/theoncologist.2015-0110

29. Planey AM, Spees LP, Biddell CB, et al. The intersection of travel burdens and financial hardship in cancer care: a scoping review. JNCI Cancer Spectr. 2024;8(5):pkae093. doi:10.1093/jncics/pkae093

30. Keating NL, Brooks GA, Landrum MB, et al. The Oncology Care Model and Adherence to Oral Cancer Drugs: A Difference-in-Differences Analysis. J Natl Cancer Inst. 2022;114(6):871-877. doi:10.1093/jnci/djac026

31. Davis TC, Arnold CL, Mills G, et al. Assessment of Oral Chemotherapy Nonadherence in Chronic Myeloid Leukemia Patients Using Brief Measures in Community Cancer Clinics: A Pilot Study. Int J Environ Res Public Health. 2021;18(21):11045. doi:10.3390/ijerph182111045