CML-644

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Treatment patterns and adverse events among elderly newly diagnosed patients with chronic myeloid leukemia: A real-world analysis of the Medicare Fee-for-Service population

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KEY FINDINGS & CONCLUSIONS

- Most CML patients receiving 1G or 2G as their first TKI experienced treatment switches, dose reductions, high treatment discontinuations, and high prevalence of AEs
- Patients treated with 2G TKIs had shorter median time on treatment and a greater proportion of treatment discontinuation and treatment switching compared to patients with 1G TKI
- There remains a substantial unmet need for more tolerable treatment options in newly diagnosed elderly patients with CML

LIMITATIONS

- The study is subject to common limitations that are inherent to retrospective observational studies using claims data, and results may not be generalizable to beneficiaries with other insurance types and/or un-insured
- Claims databases only record diagnosis and procedure codes that were used for reimbursement purposes, reasons for treatment modifications were not recorded. Precise estimates of the timing of treatment modifications were limited as the outcome definitions were based on how the data were collected, such as different recorded doses or gaps between prescription refills

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INTRODUCTION

- Chronic myeloid leukemia (CML) is a hematological malignancy characterized by aberrant BCR-ABL1 gene fusion[1]
- Tyrosine kinase inhibitors (TKIs) are the mainstay of CML treatment, however, intolerance to TKIs remains a problem with patients often requiring TKI switches[2,3]
- Second generation (2G) TKIs are often associated with greater toxicity.[4] Because older adults typically have more comorbidities and may be less able to tolerate 2G TKIs, they often receive first generation (1G) TKI
- While the average onset age is 64,[5] older patients are underrepresented in clinical studies and real-world analyses.[6-8] Additionally, adverse events (AEs) in real-world settings have not been adequately studied
- The objective of this study was to describe treatment patterns and prevalence of AEs – stratified by TKI generations - 1G or 2G - among newly diagnosed elderly CML patients (≥65 years) who received their first TKI in a real-world setting

METHODS

- This was a descriptive retrospective analysis of elderly patients with CML who received TKIs, using the US Centers for Medicare and Medicaid Services 100% Medicare Fee-for-Service database
- The study included patients with a CML diagnosis between January 1, 2016, through December 31, 2022 (observation period) who initiated a TKI within 3 months after the first observed CML diagnosis (**Figure 1**)
- Index date was defined as the start date of first TKI therapy with an index identification period from January 1, 2017, and June 30, 2022. Patients were required to have ≥12 months of continuous enrollment (Parts A, B, and D) prior to index (baseline period) and ≥6 months continuous enrollment post-index (follow-up period, including index date)
- The duration of index treatment was defined as the time from treatment initiation (index date) to the first occurrence of either treatment discontinuation or date of censoring (end of continuous enrollment, or study period, whichever occurs first)
- **Treatment discontinuation** was defined as the earliest occurrence of the following: 1) ≥90-day gap in CML treatment with no resumption of that treatment after the gap, 2) **treatment switch** defined as initiation of another CML-related treatment including other TKIs of interest or omacetaxine, 3) death, 4) hematopoietic stem cell transplantation (HSCT)
- **Temporary interruption** was defined as ≥90-day gap in CML treatment followed by resumption of that treatment after the gap
- **Dose reduction** was defined as any prescription with a dose lower than the index prescription dose
- The prevalence of AEs were reported as defined by ≥1 ICD-10-CM diagnosis code for a relevant AE during the follow-up period of first TKI therapy

RESULTS

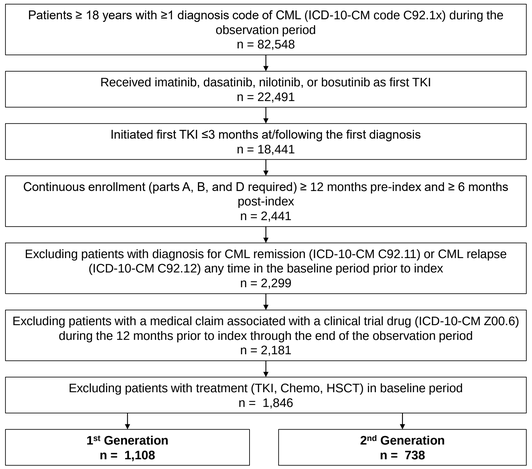
Patient attrition

- Overall, 1,846 elderly patients with CML initiated treatment with a TKI: 60% (n=1,108) with 1G TKI (imatinib) and 40% (n=738) with 2G TKI (dasatinib, nilotinib, or bosutinib) (**Figure 1**)

Baseline demographics and clinical characteristics

- Median age was 75 years for those treated with 1G TKI and 73 years for those treated with a 2G TKI. Most patients were White (1G: 90.5%; 2G: 91.3%), and there was a similar proportion of males (1G: 53.2%, 2G: 55.6%) between groups. The NCI comorbidity index was higher in patients treated with 1G TKI versus 2G TKIs (0.7 vs 0.6) (**Table 1**)
- Darkow CML disease complexity[9] was similar between groups, with similar proportions classified as Moderate (1G: 47.0%; 2G: 46.1%) and Severe (1G: 29.7%; 2G: 32.5%)
- Median follow-up time was similar between groups (1G: 27.3 months; 2G: 29.5 months)
- Distance between prescriber and patient was greater than 25 miles for 24.9% of patients treated with 1G TKI and 22.9% of patients treated with 2G TKI

Figure 1. Patient sample attrition



Abbreviations: CML, chronic myeloid leukemia; **HSCT,** hematopoietic stem cell transplantation; **ICD-10-CM**, International Classification of Diseases, 10th Revision, Clinical Modification; **TKI,** tyrosine kinase inhibitor

Treatment patterns

- The mean time on treatment was 18.5 months for 1G patients and 14.4 months for 2G patients (**Table 2**)
- Among 1G patients, 56.4% had treatment discontinuation (including 22.9% with treatment switch), 28.6% had dose reduction, and 11.1% had temporary treatment interruption (**Figure 2**)
- Among 2G patients, 70.3% had treatment discontinuation (including 35.1% with treatment switch), 29.7% had dose reduction, and 9.9% had temporary treatment interruption (**Figure 2**)

AEs with a prevalence ≥10%

- The most common AEs by prevalence included hypertension, anemia, abnormal glucose, fatigue, peripheral edema, and pleural effusion (**Figure 3**)

Table 1. Baseline demographics and clinical characteristics

Characteristic	1st Generation (n=1,108)	2nd Generation (n=738)
Age at index, years		
Median (Q1, Q3)	75.0 (70.0, 81.0)	73.0 (69.0, 78.0)
Sex, n (%)		
Male	589 (53.2)	410 (55.6)
Female	519 (46.8)	328 (44.4)
Race[a], n (%)		
White	1,003 (90.5)	674 (91.3)
Black	48 (4.3)	32 (4.3)
Other/Unknown	38 (3.4)	19 (2.6)
Geographic Region, n (%)		
South	406 (36.6)	325 (44.0)
Midwest	269 (24.3)	141 (19.1)
Northeast	260 (23.5)	139 (18.8)
West/Other	173 (15.6)	133 (18.0)
Index Year, n (%)		
2017	201 (18.1)	112 (15.2)
2018	189 (17.1)	146 (19.8)
2019	190 (17.1)	120 (16.3)
2020	195 (17.6)	144 (19.5)
2021	233 (21.0)	145 (19.6)
2022	100 (9.0)	71 (9.6)
NCI Comorbidity Index		
Median (Q1, Q3)	0.7 (0.3, 1.3)	0.6 (0.3, 1.0)
Darkow CML Disease Complexity, n (%)		
Mild	258 (23.3)	158 (21.4)
Moderate	521 (47.0)	340 (46.1)
Severe	329 (29.7)	240 (32.5)
Follow-up duration from index, months		
Median (Q1, Q3)	27.3 (16.0, 43.9)	29.5 (16.3, 46.0)
Distance between prescriber and patient[b], n (%)	**1st Generation (n=1,103)**	**2nd Generation (n=734)**
<1 mile	122 (11.1)	91 (12.4)
Drivable distance (>1-25 miles)	706 (64.0)	475 (64.7)
Inconvenient distance (>25-75 miles)	181 (16.4)	108 (14.7)
Long distance (>75 miles)	94 (8.5)	60 (8.2)

[a]Data for the Race categories of Hispanic, Asian, and North American Native were not included because the data was masked to protect patient confidentiality [b]Distance was calculated as a straight line from prescriber to patient, information was not available for all patients
Abbreviations: CML, chronic myeloid leukemia; **NCI**, National Cancer Institute; **Q1**, first quartile; **Q3**, third quartile

Table 2. Treatment patterns

First TKI received, n (%)	1st Generation (n=1,108)	2nd Generation (n=738)
Imatinib	1,108 (100%)	-
Dasatinib	-	550 (74.5%)
Nilotinib	-	139 (18.8%)
Bosutinib	-	49 (6.6%)
Time on first TKI treatment (months), mean (SD)	18.5 (16.9)	14.4 (14.9)

Abbreviations: SD, standard deviation; **TKI**, tyrosine kinase inhibitor

Figure 2. Treatment modification

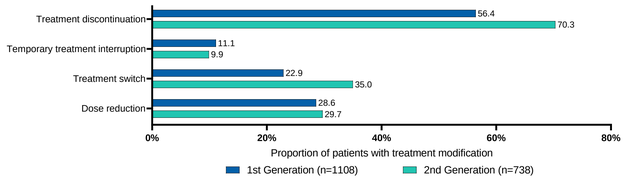
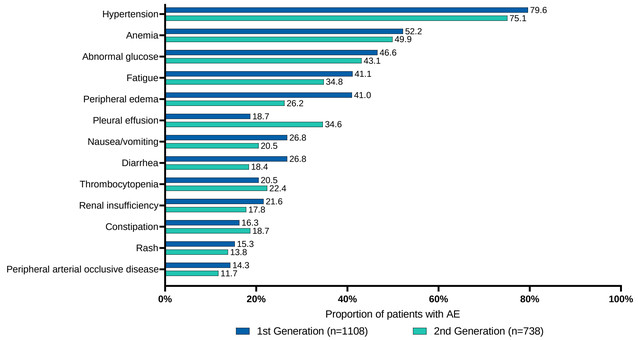


Figure 3. AEs with a prevalence ≥10%



AEs are subject to over representation due to pre-existing comorbidities, particularly common chronic diseases including hypertension and diabetes
Abbreviations: AE, adverse event

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