Poster CML-205

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Non-optimal treatment in patients with newly diagnosed chronic myeloid leukemia in chronic phase treated with tyrosine kinase inhibitors in the United States: a claims data analysis

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KEY FINDINGS & CONCLUSIONS

- In this real-world study using a conservative approach to assess non-optimal treatment in early lines of therapy for CML, findings showed that about one-quarter of patients with CML-CP treated with TKI experienced early treatment modifications or low adherence, with more pronounced rates in 2L
- This suggests that unmet clinical needs persist in this population of patients with CML-CP receiving 1L and 2L TKI and are as important for patients treated with 1G or 2G (mainly dasatinib) TKI, and that patients may benefit from new treatment options with better efficacy and tolerability profiles
- Future studies are needed to assess the impact of NOPT on molecular responses and quality of life of CML patients

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BACKGROUND AND OBJECTIVES

- Treatment options for patients with chronic myeloid leukemia in chronic phase (CML-CP) include first-generation (1G) tyrosine kinase inhibitor (TKI) imatinib and second-generation (2G) TKIs dasatinib, nilotinib, or bosutinib for first-line (1L) and second-line (2L) treatment, with the allosteric inhibitor targeting ABL1 myristoyl pocket asciminib and the third-generation TKI ponatinib as additional treatment options for those with the T315I mutation[1]
- While 1G and 2G TKIs are effective in early lines for CML-CP, patients may experience intolerance or resistance to TKIs leading to non-optimal treatment (NOPT)[2-4]
- This study assessed NOPT in patients with CML receiving 1L and 2L TKI therapies in the United States (US)

METHODS

Data Source

- This study used Optum's de-identified Clinformatics® Data Mart Database (01/01/2007-06/30/2022)
- The database contains the enrollment history as well as pharmacy and medical claims for over 15 million beneficiaries in the US in any given year
- The data are de-identified and comply with the confidentiality requirements of the Health Insurance Portability and Accountability Act

Study Design

- A retrospective, non-interventional cohort study design was used
- The ***observation period*** spanned from the start of data availability to the earliest of end of data, end of continuous health plan coverage, or death (if available)
- The ***1L/2L index date*** was defined as the date of the first claim for 1L/2L TKI therapy
- The ***baseline period*** was defined as the 6 months before the index date
- The ***follow-up period*** spanned from the index date to the earliest of end of observation period, or hematopoietic stem cell transplantation (HSCT)

Sample Selection

- Adult patients with CML who initiated 1L TKI therapy (imatinib, dasatinib, nilotinib, or bosutinib) on or after 2012 were included in the ***1L TKI cohort***
- Adult patients with CML who initiated 2L TKI therapy (imatinib, dasatinib, nilotinib, bosutinib, or ponatinib) on or after 2012 were included in the ***2L TKI cohort***
- In both cohorts, patients were required to have ≥2 years of follow-up, and ***1G*** and ***2G TKI subgroups*** were defined based on the index TKI

Measure, Outcomes and Statistical Analysis

- NOPT base-case and sensitivity definitions are illustrated in **Figure 1**
- Proportion of patients with NOPT were reported for each of the **1L** and **2L TKI cohorts**, overall, and by **1G** and **2G TKI subgroups**

RESULTS

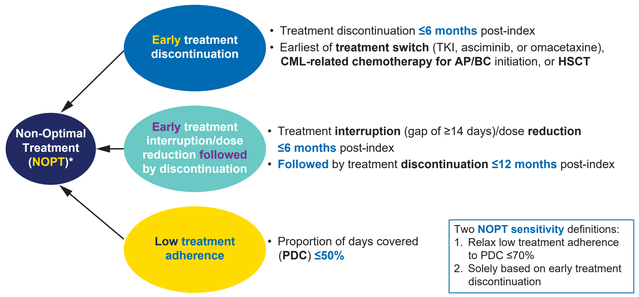
Study Sample

- A total of 881 patients were included in the **1L TKI cohort**, among them 408 (46.3%) initiated a 1G TKI and 473 (53.7%) initiated a 2G TKI (dasatinib: 31.3%, nilotinib: 21.1%, bosutinib: 1.2%)
- A total of 247 patients were included in the **2L TKI cohort**, among them 62 (25.1%) initiated a 1G TKI, 182 (73.7%) initiated a 2G TKI (dasatinib: 32.4%, nilotinib: 27.9%, bosutinib: 13.4%), and 3 (1.2%) initiated ponatinib

Patient Characteristics

- Among patients in the **1L TKI cohort**, mean (SD) age was 62.6 (15.4) years, 46.1% were female, 72.5% were White, and 53.6% were insured through a Medicare Advantage plan operated by commercial insurance (Part C) (**Table 1**)
- Among patients in the **2L TKI cohort**, mean (SD) age was 64.2 (15.5) years, 49.0% were female, 74.1% were White, and 55.5% were insured through a Medicare Advantage plan operated by commercial insurance (Part C) (**Table 1**)

Figure 1. NOPT definition



*Criteria are not mutually exclusive.

Non-Optimal Treatment (NOPT)

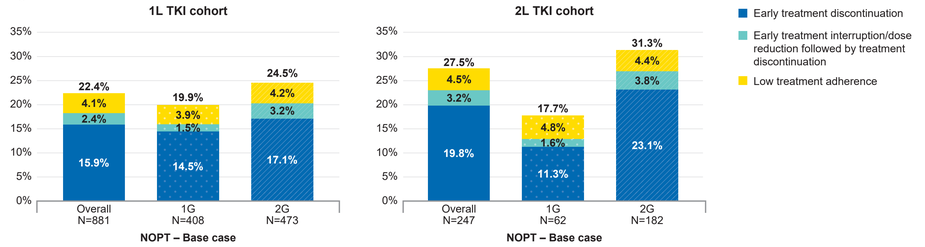
- Among the **1L TKI cohort**, 197 patients (22.4%) were classified as having NOPT according to the base case definition (**Figure 2**); Of these, 81 (41.1%) received a 1G TKI and 116 (58.9%) received a 2G TKI (dasatinib: 38.6%, nilotinib: 18.8%, bosutinib: 1.5%)
  - In Sensitivity 1, 265 patients (30.1%) of the **1L TKI cohort** were classified as having NOPT (1G: 26.5%, 2G: 33.2%) and in Sensitivity 2, 140 patients (15.9%) were classified as having NOPT (1G: 14.5%, 2G: 17.1%)
- Among the **2L TKI cohort**, 68 patients (27.5%) were classified as having NOPT according to the base case (**Figure 2**); Of these, 11 (16.2%) received a 1G TKI and 57 (83.8%) received a 2G TKI (dasatinib: 36.8%, nilotinib: 33.8%, bosutinib: 13.2%)
  - In Sensitivity 1, 87 patients (35.2%) of the **2L TKI cohort** were classified as having NOPT (1G: 30.6%, 2G: 37.4%) and in Sensitivity 2, 49 patients (19.8%) were classified as having NOPT (1G: 11.3%, 2G: 23.1%)
- In the base case, the most common indicator of NOPT for TKIs was early treatment discontinuation in both **1L** and **2L TKI cohorts** (15.9% and 19.8%, respectively) followed by PDC ≤50% (4.1% and 4.5%) and early temporary treatment interruption and/or dose reduction followed by treatment discontinuation (2.4% and 3.2%) (**Figure 2**)
- Trends were consistent between **1G** and **2G TKI subgroups** in both **1L** and **2L TKI cohorts**

Table 1. Baseline Demographic and Clinical Characteristics in 1L and 2L TKI Cohorts

	1L TKI Cohort			2L TKI Cohort		
	Overall N = 881	1G N = 408	2G N = 473	Overall N = 247	1G N = 62	2G N = 182
At index date						
Index treatment[1]						
Imatinib	408 (46.3%)	408 (100.0%)	0 (0.0%)	62 (25.1%)	62 (100.0%)	0 (0.0%)
Dasatinib	276 (31.3%)	0 (0.0%)	276 (58.4%)	80 (32.4%)	0 (0.0%)	80 (44.0%)
Nilotinib	186 (21.1%)	0 (0.0%)	186 (39.3%)	69 (27.9%)	0 (0.0%)	69 (37.9%)
Bosutinib	11 (1.2%)	0 (0.0%)	11 (2.3%)	33 (13.4%)	0 (0.0%)	33 (18.1%)
Age, years; Mean ± SD [Median]	62.6 ± 15.4 [66.0]	63.5 ± 15.6 [67.0]	61.9 ± 15.3 [65.0]	64.2 ± 15.5 [69.0]	69.4 ± 13.2 [72.0]	62.8 ± 15.8 [67.0]
≥65 years old, N (%)	458 (52.0%)	217 (53.2%)	241 (51.0%)	144 (58.3%)	46 (74.2%)	98 (53.8%)
Female, N (%)	406 (46.1%)	180 (44.1%)	226 (47.8%)	121 (49.0%)	33 (53.2%)	86 (47.3%)
Race/ethnicity, N (%)						
White	639 (72.5%)	288 (70.6%)	351 (74.2%)	183 (74.1%)	53 (85.5%)	130 (71.4%)
Black	78 (8.9%)	43 (10.5%)	35 (7.4%)	23 (9.3%)	<5	21 (11.5%)
Hispanic	89 (10.1%)	40 (9.8%)	49 (10.4%)	18 (7.3%)	<5	13 (7.1%)
Asian	40 (4.5%)	16 (3.9%)	24 (5.1%)	13 (5.3%)	<5	9 (4.9%)
Unknown	35 (4.0%)	21 (5.1%)	14 (3.0%)	10 (4.0%)	0 (0.0%)	9 (4.9%)
Census region of residence[2], N (%)						
Midwest	216 (24.5%)	103 (25.2%)	113 (23.9%)	65 (26.3%)	18 (29.0%)	47 (25.8%)
Northeast	96 (10.9%)	48 (11.8%)	48 (10.1%)	30 (12.1%)	9 (14.5%)	21 (11.5%)
West	219 (24.9%)	98 (24.0%)	121 (25.6%)	70 (28.3%)	12 (19.4%)	56 (30.8%)
South	345 (39.2%)	157 (38.5%)	188 (39.7%)	82 (33.2%)	23 (37.1%)	58 (31.9%)
Health plan type, N (%)						
Commercial insurance with Medicare advantage plan	472 (53.6%)	228 (55.9%)	244 (51.6%)	137 (55.5%)	44 (71.0%)	92 (50.5%)
Commercial insurance only	409 (46.4%)	180 (44.1%)	229 (48.4%)	110 (44.5%)	18 (29.0%)	90 (49.5%)
Calendar year of index date, N (%)						
2012 – 2015	353 (40.0%)	144 (35.3%)	209 (44.3%)	96 (38.9%)	22 (35.5%)	71 (38.9%)
2016 – 2018	343 (39.0%)	171 (41.9%)	172 (36.4%)	96 (38.9%)	26 (41.9%)	70 (38.5%)
2019 – 2022	185 (21.0%)	93 (22.8%)	92 (19.4%)	55 (22.3%)	14 (22.6%)	41 (22.5%)
During the 6-month baseline period						
NCI Comorbidity Index; Mean ± SD [Median]	0.4 ± 0.5 [0.3]	0.4 ± 0.5 [0.3]	0.4 ± 0.5 [0.3]	0.5 ± 0.6 [0.3]	0.7 ± 0.6 [0.6]	0.4 ± 0.6 [0.3]
0, N (%)	396 (44.9%)	173 (42.4%)	223 (47.1%)	105 (42.5%)	15 (24.2%)	87 (47.8%)
(0-1), N (%)	369 (41.9%)	177 (43.4%)	192 (40.6%)	99 (40.1%)	29 (46.8%)	70 (38.5%)
> 1, N (%)	116 (13.2%)	58 (14.2%)	58 (12.2)	43 (17.4%)	18 (29.0%)	25 (13.7%)
Darkow Disease Complexity Index, N (%)						
Mild	353 (40.1%)	182 (44.6%)	171 (36.2%)	85 (34.4%)	16 (25.8%)	69 (37.9%)
Moderate	342 (38.8%)	146 (35.8%)	196 (41.4%)	97 (39.3%)	29 (46.8%)	67 (36.8%)
Severe	186 (21.1%)	80 (19.6%)	106 (22.4%)	65 (26.3%)	17 (27.4%)	46 (25.3%)
Time between index date and end of observation period, months; Mean ± SD [Median]	53.6 ± 24.2 [47.7]	52.1 ± 22.8 [45.4]	54.9 ± 25.3 [49.6]	50.8 ± 22.0 [44.4]	52.0 ± 21.5 [47.1]	50.6 ± 22.2 [44.1]

Abbreviations: 1G: 1st generation; 2G: 2nd generation; 1L: first-line; 2L: second-line; SD: standard deviation; TKI: tyrosine kinase inhibitors.
Notes: [1] <5 patients received ponatinib as their 2L TKI. [2] Patients unaccounted for had a census region of residence listed as "unknown".

Figure 2. Patients with NOPT[1]



Abbreviations: 1G: 1st generation; 2G: 2nd generation; 1L: first-line; 2L: second-line; N: number; NOPT: non-optimal treatment; PDC: proportion of days covered, TKI: tyrosine kinase inhibitors.
Note: [1] Percentages were assessed in the following order of priority: 1) Early treatment discontinuation, 2) Early treatment interruption/dose reduction followed by treatment discontinuation, and 3) Low treatment adherence.

Limitations

- Diagnosis and procedure codes are recorded for reimbursement purposes in administrative claims databases and may be subject to coding errors or data omissions
- Since TKI use was identified based on pharmacy claims for prescription fills, actual medication consumption could not be guaranteed
- CML phase, Eastern Cooperative Oncology Group performance status, Sokal scores, lab test results (e.g., molecular responses and mutations), and reasons for diagnosis or procedure codes/treatment modifications (e.g., TKI resistance or intolerance) were not available

References
1. Jabbour E, et al. *Am J Hematol.* 2022;97(9):1236-1256. **2.** Gambacorti-Passerini C, et al. *Eur J Haematol.* 2021;106(1):82-89. **3.** Lahaye T, et al. *Cancer.* 2005;103(8):1659-1669. **4.** Hehlmann R, et al. *Am J Hematol.* 2019;94(1):46-54.

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