Poster CML-475

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Real-World Treatment Patterns Among Patients with Chronic Myeloid Leukemia in Chronic Phase Cycling Through Multiple Tyrosine Kinase Inhibitors in the United States

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BACKGROUND

- Tyrosine kinase inhibitors (TKIs) that target the BCR-ABL1 oncoprotein are the standard of care for chronic myeloid leukemia (CML); these include first generation (1G; imatinib), second generation (2G; dasatinib, nilotinib, and bosutinib), and third generation (3G; ponatinib) TKIs[1,2]
- Despite the advances in therapy since the introduction of 2G and 3G TKIs, a proportion of patients with CML in the chronic phase (CML-CP) are refractory or intolerant to these medications and cycle through multiple lines of therapy, reaching third line or later (3L+)[3]
- More recently, asciminib, a selective allosteric inhibitor, has been approved for adult patients with CML-CP who were previously treated with two or more TKIs or who have the T315I mutation[4]. This study was conducted prior to asciminib approval
- There is limited information describing real-world treatment patterns and clinical outcomes for patients with CML-CP who cycle through multiple lines of therapy

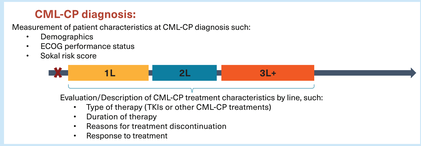
OBJECTIVES

- This study assessed the real-world treatment patterns of patients with CML-CP who reached 3L+ in the United States (US)

METHODS

- This study was a retrospective physician panel-based chart review study in the US
- Between March 5, 2021 and June 14, 2021, de-identified patient-level data were retrospectively collected from patient clinical charts via an online case report form completed by US hematologists/oncologists
- Respondents were from an existing panel of physicians with experience treating patients with CML-CP from various practice settings (e.g., community and academic practices) and from all US census regions
- Physicians were eligible to participate in the study if they were responsible for treatment decisions and follow-up of ≥ 1 adult patient with CML-CP
- Eligible medical charts included those of adult patients with CML-CP who initiated a first-line (1L) therapy, switched to a second-line (2L) therapy, and subsequently switched to 3L therapy between January 1, 2013 and November 30, 2018, with ≥24 months of follow-up after 3L initiation, except if the patient died within that period post 3L initiation
- Patients were included if they received all lines of therapy for CML-CP (TKIs or other CML-CP treatments) outside of an interventional clinical trial setting
- Data were collected on physician practices, patient demographic and clinical characteristics, and CML-CP treatment characteristics including reasons for line of treatment discontinuation (based on physicians' interpretation) and response to treatment
- Patient characteristics were measured at CML-CP diagnosis; treatment patterns for CML-CP were evaluated/described from 1L to 3L+ (**Figure 1**)
- All analyses were descriptive and reported using frequencies, proportions, means, standard deviations, and medians
- Institutional review board exemption from a full review was obtained from the WCG Independent Review Board

Figure 1. Study design



1L / 2L / 3L: first-line / second-line / third-line; CML-CP, chronic myeloid leukemia; ECOG, Eastern Cooperative Oncology Group; TKI, tyrosine kinase inhibitor

RESULTS

Physician characteristics

- A total of 64 physicians provided data for 164 patients with CML-CP who initiated 3L+
- Nearly two-thirds of physicians (64%) were from community-based practices; the remaining 36% were from academic-based practices
- One-third of physicians (33%) had primary practice located in South, 27% in Northeast, 20% in West, and 20% in Midwest US census regions
- More than half of physicians (56%) were from large primary practices (≥10 physicians) located in urban areas (56%)

Patient characteristics

- The mean age at CML-CP diagnosis was 57 years, with 32% of patients aged 65 years or older and 55% were male (**Table 1**)
- At CML-CP diagnosis, 47% and 13% of patients had an intermediate and high Sokal risk score, respectively
- Most patients had ECOG performance grade 0 (40%) or grade 1 (48%) at CML-CP diagnosis

Table 1. Demographic and Clinical Characteristics at CML-CP Diagnosis

	N=164
Age (years), mean ± SD [median]	57.6 ± 12.3 [58.0]
≥ 65 years, n (%)	53 (32.3%)
Male, n (%)	91 (55.5%)
Race/ethnicity, n (%)	
White - Non-Hispanic/Latino	107 (65.2%)
Black or African American - Non-Hispanic/Latino	25 (15.2%)
Hispanic/Latino	17 (10.4%)
East Asian	8 (4.9%)
Asian Indian	6 (3.7%)
North American Native	1 (0.6%)
Insurance type, n (%)[1]	
Commercial/private insurance	103 (62.8%)
Medicare	51 (31.1%)
Medicaid	20 (12.2%)
Other/unknown	2 (1.2%)
Year of CML-CP diagnosis, n (%)	
2000-2004	4 (2.4%)
2005-2009	3 (1.8%)
2010-2014	87 (53.0%)
2015-2018	70 (42.7%)
Sokal risk score, n (%)	
Low-risk (< 0.8)	46 (28.0%)
Intermediate-risk (0.8 – 1.2)	77 (47.0%)
High-risk (> 1.2)	22 (13.4%)
ECOG performance status, n (%)	
Grade 0 – 1	144 (87.8%)
Grade 2+	20 (12.2%)

CML-CP, chronic myeloid leukemia in chronic phase; ECOG, Eastern Cooperative Oncology Group; SD, standard deviation
[1]Physicians could select more than one option (not mutually exclusive).

CML-CP treatment characteristics

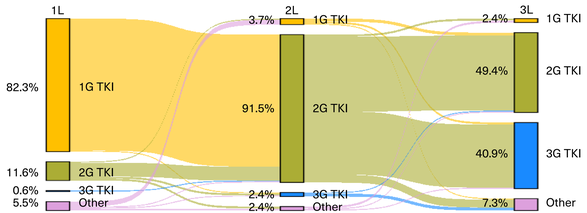
- In 1L (median duration: 12.9 months), most patients (82%) received a 1G TKI and 12% received a 2G TKI (**Table 2**)
- In 2L (median duration: 11.9 months), most patients (92%) received a 2G TKI
- In 3L (median duration: 32.6 months), 2% of patients received a 1G TKI, 49% received a 2G TKI, 41% received a 3G TKI, and 7% received other CML-CP treatments; at data collection, most patients (67%) were undergoing 3L treatment
- Patients mainly cycled from the 1G TKI in 1L to a 2G TKI in 2L (81%), and from 2L to 3L, 46% cycled between 2G TKIs and 39% switched from a 2G TKI to a 3G TKI (**Figure 2**)
- The most commonly observed treatment sequences from 1L to 3L were: imatinib → dasatinib → nilotinib (17%), imatinib → dasatinib → ponatinib (15%), and imatinib → nilotinib → ponatinib (12%)
- The most common reasons for treatment discontinuation in earlier lines, based on physicians' interpretation, were lack of efficacy (1L: 34%; 2L: 26%), resistance (both 1L and 2L: 27%), and intolerance (1L: 21%; 2L: 26%; **Figure 3**)
- The proportion of patients with a last molecular response (MR; achieved and sustained) of MR2 or better was 44% in 1L and 53% in 2L, and MR3 or better was 32% in both lines (**Figure 4**)

Table 2. Treatment Characteristics by Line of Therapy for CML-CP

	N=164		
	1L	2L	3L[1]
Medications used, n (%)			
Imatinib	135 (82.3%)	6 (3.7%)	4 (2.4%)
Dasatinib	15 (9.1%)	77 (47.0%)	17 (10.4%)
Nilotinib	4 (2.4%)	51 (31.1%)	31 (18.9%)
Bosutinib	0 (0.0%)	22 (13.4%)	33 (20.1%)
Ponatinib	1 (0.6%)	4 (2.4%)	67 (40.9%)
Other[2]	9 (5.5%)	4 (2.4%)	12 (7.3%)
Duration of line (months), mean ± SD [median]	19.8 ± 20.7 [12.9]	16.0 ± 13.2 [11.9]	35.1 ± 22.7 [32.6]
Time between termination of 1L and start of 2L (days)	45.7 ± 137.1 [10.0]		N/A
Time between termination of 2L and start of 3L (days)	N/A	66.0 ± 166.8 [13.0]	

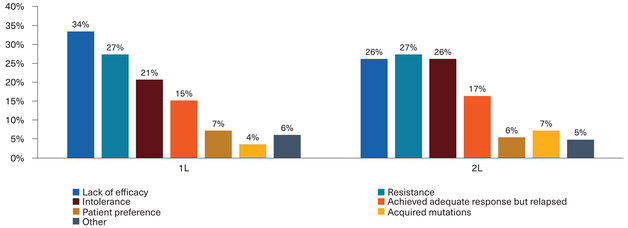
1L / 2L / 3L, first-line / second-line / third-line; CML-CP, chronic myeloid leukemia in chronic phase; N/A, not available; SD, standard deviation
[1]Fifteen patients were observed with a fourth-line (4L) therapy and 3 with a fifth-line (5L) therapy.
[2]Other CML-CP treatments included in 1L hydroxyurea monotherapy, in 2L/3L omacetaxine, interferon, and hydroxyurea monotherapy.

Figure 2. CML-CP Treatment Patterns (N=164)[1,2]



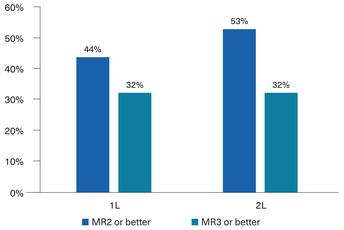
1L / 2L / 3L, first-line / second-line / third-line; TKI, tyrosine kinase inhibitor
[1]1G TKIs included only imatinib. 2G TKIs included only dasatinib, nilotinib, and bosutinib. 3G TKIs included only ponatinib.
[2]Other CML-CP treatments included in 1L hydroxyurea monotherapy, in 2L/3L omacetaxine, interferon, and hydroxyurea monotherapy.

Figure 3. Reasons for Treatment Discontinuation in Earlier Lines of Therapy for CML-CP (N=164)[1,2]



1L / 2L, first-line / second-line; CML-CP, chronic myeloid leukemia in chronic phase
[1]Physicians could select more than one option (not mutually exclusive).
[2]Other reasons for treatment discontinuation included inconvenient treatment administration/non-adherence, drug-drug interactions, pregnancy or planning to become pregnant, economic reasons, or unknown/not sure.

Figure 4. Last Molecular Response Achieved in Earlier Lines of Therapy for CML-CP (N=164)[1,2]



1L / 2L, first-line / second-line; CML-CP, chronic myeloid leukemia in chronic phase; MR, molecular response
[1]Achieved and sustained MR was assessed based on the last measurement in the line of therapy.
[2]MR2 was defined as BCR-ABL1/ABL1 ≤ 1% OR a 2-log reduction. MR3 was defined as BCR-ABL1/ABL1 ≤ 0.1% OR a 3-log reduction.

CONCLUSIONS

- Patients with CML-CP in 3L+ have rapidly cycled between 1G TKI and 2G TKI in 1L and 2L
- Rates of MR3 did not improve between earlier lines for CML-CP, with lack of efficacy/resistance being the most common reasons for discontinuation; intolerance became more important in 2L
- Findings highlight the need for novel therapeutics with improved safety/efficacy to prolong treatment to improve response in earlier lines and for patients in later lines who exhaust treatment options quickly

LIMITATIONS

- CML treatment management and monitoring in real-world settings may be based on heterogeneous criteria and assessment schedules
- It is unclear how generalizable these findings are to the overall practice in the US
- By design, patients with CML-CP who reached 3L+ were included in this study; patients who progressed to advanced CML phases or died prior to 3L with an unmet treatment need in earlier lines were not captured
- The results may be subject to limitations inherent of retrospective chart reviews, including potential missing/not well-recorded data in patient medical charts

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