Poster CML-317

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Asciminib after two or more prior tyrosine kinase inhibitors in chronic myeloid leukemia: real-world evaluation of treatment patterns and clinical outcomes in US clinical practice

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KEY FINDINGS & CONCLUSIONS

- This is the first real-world study describing treatment patterns and clinical outcomes among patients with Ph+ CML-CP treated with asciminib in the US
- Treatment persistence for asciminib remained high at 24-weeks post-index
- The findings of real-world treatment efficacy based on achieving BCR::ABL1 ≤0.1% were consistent with the ASCEMBL trial[4]
- Patients who initiated asciminib after 2 prior TKIs had descriptively higher persistence and treatment response rates than those initiated on asciminib after ≥3 prior TKIs
- For patients without BCR::ABL1 ≤0.1% prior to asciminib initiation, 32.9% achieved **BCR::ABL1 ≤0.1%** by 24-weeks
- For patients without BCR::ABL1 ≤1% prior to asciminib initiation, 46.3% achieved **BCR::ABL1 ≤1%** by 24-weeks
- Further studies are warranted to assess long-term effectiveness of asciminib in the real-world setting

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INTRODUCTION

- Tyrosine kinase inhibitors (TKIs) are the mainstay of treatment for patients with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia in chronic phase (CML-CP)[1]
- Asciminib, a first-in-class inhibitor to Specifically Target the ABL Myristoyl Pocket (STAMP), received accelerated FDA approval on October 29th, 2021, for the treatment of adult patients with Ph+ CML-CP previously treated with two or more TKIs and full approval for patients with Ph+ CML-CP with the T315I mutation[2,3]
- Results from the Phase III ASCEMBL trial (NCT03106779) has shown that among patients with CML-CP who were previously treated with two or more TKIs, asciminib demonstrated superior efficacy (i.e., major molecular response [MMR] at 24 weeks: 24.9% for asciminib, 11.9% for bosutinib) and better safety and tolerability than bosutinib[4]
- There are limited real-world data on patients with Ph+ CML-CP treated with asciminib in the US

OBJECTIVES

- To describe treatment patterns and clinical outcomes among patients with Ph+ CML-CP who initiated asciminib after treatment with two or more TKIs in the US clinical practice

METHODS

Data source

- Data between January 1st, 2011 and November 30th, 2022 from patients with CML-CP who initiated asciminib were obtained from the US Nationwide Flatiron Health oncology electronic health record (EHR)-derived de-identified database, a longitudinal database comprising patient-level structured and unstructured data, curated via technology-enabled abstraction.[5,6] originating from ~280 cancer clinics (~800 sites of care)
- Data were Health Insurance Portability and Accountability Act (HIPAA) compliant

Study design

- A retrospective, non-interventional longitudinal study cohort was used
- Asciminib initiation following an initial CML diagnosis and two or more TKI treatments was defined as the **index date**
- Baseline patient characteristics were evaluated from initial CML diagnosis up to the index date (excluded)
- The **observation period** spanned from the index date to the earliest of stem-cell transplant (SCT), death, loss-to-follow (i.e., last activity in EHR), or end of data availability (**end of observation period**)

Study sample

- Patients were included in the study if they met all the following inclusion criteria:
  - Had ≥1 diagnosis for CML on or after January 1st, 2011 in the EHR (International Classification of Disease, 9th/10th Edition, Clinical Modification codes: ICD-9-CM 205.1x/ICD-10-CM C92.1x, C92.2x) AND diagnosed with Ph+ CML-CP, as confirmed through chart abstraction
  - Had evidence of treatment with asciminib on or after October 29th, 2021 (i.e., asciminib FDA approval date), as confirmed through chart abstraction
  - Initiated asciminib following use of two or more prior TKIs
- Patients were excluded if they met any of the following exclusion criteria:
  - Had no clinical activity (e.g., medical visit, medication order) in EHR within 6 months of the index date
  - Had evidence of accelerated phase or blast crisis (AP/BC) prior to the index date
  - Had an SCT prior to the index date
  - Had positive test for T315I mutation at any time
  - Received a clinical study drug between November 15th, 2017 and December 4th, 2019 (randomization dates for ASCEMBL trial)[3]

Measures and study outcomes

- Treatment discontinuation: Time-to-treatment discontinuation (TTD) was defined as the time from the index date until treatment end date with asciminib (event; as confirmed through chart abstraction based on clinician-anchored assessment) or the end of the observation period (censor)
- Molecular response (MR): Time-to-BCR::ABL1 ≤0.1% and time-to-BCR::ABL1 ≤1%, separately
  - Time-to-MR was defined as the time from the index date until first MR assessment with BCR::ABL1 ≤0.1% (BCR::ABL1 ≤1%) (event) or the end of the observation period (censor)
  - Patients were required to have ≥1 MR assessment during the observation period, as confirmed through chart abstraction
  - A **sensitivity analysis** was conducted for time-to-BCR::ABL1 ≤0.1% (time-to-BCR::ABL1 ≤1%) excluding patients with BCR::ABL1 ≤0.1% or better (≤1% or better) in the three months prior to the index date; as evaluated in the ASCEMBL trial[4]

Statistical analyses

- All analyses were descriptive; no statistical comparisons were performed
- TTD and time-to-MR were assessed using Kaplan-Meier (KM) analyses
- Study outcomes were assessed for the overall asciminib cohort, and by the number of prior TKIs used before asciminib initiation (i.e., 2 prior TKIs or ≥3 prior TKIs)

RESULTS

Patient characteristics

- A total of 97 adult patients with CML-CP who initiated asciminib after ≥2 prior TKIs were included in this study
- The median age was 63 years, 50.5% were female, 64.9% were White, 84.8% had Eastern Cooperative Oncology Group Performance Score 0-2, and 66.0% were treated in community-based practices (**Table 1**)
- Most patients were from the US South (50.0%)
- The median duration of observation from the index date was 6 months
- Forty-six patients (47.4%) initiated asciminib after 2 prior TKIs, 24 (24.7%) after 3 prior TKIs, and the remaining 27 after ≥4 prior TKIs (27.8%)

Table 1. Patient demographic and clinical characteristics

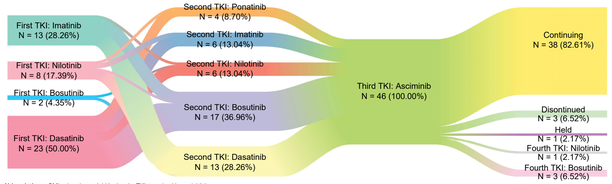
	Overall asciminib cohort N = 97	Number of prior TKIs: 2 prior TKIs N = 46	Number of prior TKIs: ≥3 prior TKIs N = 51
Age at index date, median (IQR)	63 (51, 73)	63 (45, 75)	62 (51, 71)
Female, n (%)	49 (50.5)	21 (45.7)	28 (54.9)
Race, n (%)			
White	63 (64.9)	31 (67.4)	32 (62.7)
Non-White	21 (21.6)	9 (19.6)	12 (23.5)
Unknown	13 (13.4)	6 (13.0)	7 (13.7)
Practice type,[1] n (%)			
Community	64 (66.0)	30 (65.2)	34 (66.7)
Academic	37 (38.1)	18 (39.1)	19 (37.3)
Available ECOG PS at index date, n (%)	66	32	34
0	26 (39.4)	16 (50.0)	10 (29.4)
1	30 (45.4)	12 (37.5)	18 (52.9)
≥2	10 (15.2)	4 (12.5)	6 (17.6)
Five most common baseline comorbidities, n (%)			
Other malignancies (excluding CML)	19 (19.6)	7 (15.2)	12 (23.5)
Chronic pulmonary disease	18 (18.6)	8 (17.4)	10 (19.6)
Renal disease	18 (18.6)	6 (13.0)	12 (23.5)
Congestive heart failure	16 (16.5)	7 (15.2)	9 (17.6)
Peptic ulcer disease	14 (14.4)	5 (10.9)	9 (17.6)
Last MR during last 3 months pre-index, n (%)			
BCR::ABL1 >10%	24 (24.7)	9 (19.6)	15 (29.4)
BCR::ABL1 ≤10% and >1%	18 (18.6)	9 (19.6)	9 (17.6)
BCR::ABL1 ≤1% and >0.1%	12 (12.4)	9 (19.6)	3 (5.9)
BCR::ABL1 ≤0.1% and >0.01%	12 (12.4)	9 (19.6)	3 (5.9)
BCR::ABL1 ≤0.01%	8 (8.2)	6 (13.0)	2 (3.9)
Untested/unknown	23 (23.7)	4 (8.7)	19 (37.3)
Duration of observation period, median (IQR), months	6 (3, 9)	5 (2, 7)	7 (5, 10)

Abbreviations: CML: chronic myeloid leukemia; ECOG: Eastern Cooperative Oncology Group; IQR: interquartile range; MR: molecular response; PS: performance status; TKI: tyrosine kinase inhibitor
Note:
[1] Practice type was not mutually exclusive.

Treatment patterns

- Most patients (78.4%) were prescribed 80 mg (40.2% once daily, 38.1% 40 mg twice a day) at asciminib initiation
- The use of TKIs at any time prior to asciminib initiation included dasatinib (85.6%), imatinib (63.9%), bosutinib (61.9%), nilotinib (53.6%), and ponatinib (15.5%)
- Eleven patients (9.9%) used ponatinib and 21 patients (21.6%) used dasatinib immediately prior to asciminib initiation
- Treatment sequences among patients who initiated asciminib after 2 prior TKIs (n=46) are presented in **Figure 1**
  - The most common treatment sequence was dasatinib → bosutinib → asciminib (26.1%)
- Overall, persistence rates were 85.7% by 12-weeks post-index (2 prior TKIs: 89.8%; ≥3 prior TKIs: 82.5%) and 78.1% by 24-weeks post-index (2 prior TKIs: 81.8%; ≥3 prior TKIs: 75.3%) post-index

Figure 1. Treatment sequences from CML treatment initiation among patients who initiated asciminib after two prior TKIs (N = 46)



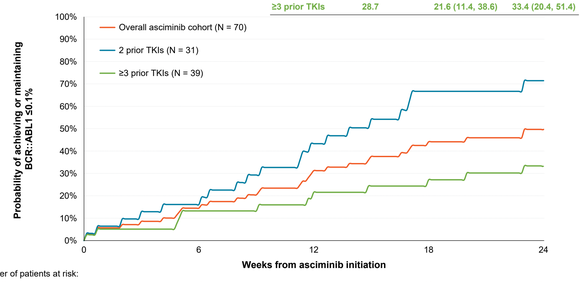
Abbreviations: CML: chronic myeloid leukemia; TKI: tyrosine kinase inhibitor

Molecular response

- Among patients with ≥1 MR test post-index (n=70), 31.3% (2 prior TKIs: 43.3%; ≥3 prior TKIs: 21.6%) and 49.7% (2 prior TKIs: 71.5%; ≥3 prior TKIs: 33.4%) achieved or maintained **BCR::ABL1 ≤0.1%** by 12- and 24-weeks, respectively (**Figure 2a**)

Figure 2a. Cumulative incidence of BCR::ABL1 ≤0.1%

	Median time to BCR::ABL1 ≤0.1%, weeks	12-week KM rate (95% CI)	24-week KM rate (95% CI)
Overall	24.1	31.3 (21.6, 43.9)	49.7 (38.1, 62.6)
2 prior TKIs	13.9	43.3 (27.8, 62.8)	71.5 (53.5, 87.1)
≥3 prior TKIs	28.7	21.6 (11.4, 38.6)	33.4 (20.4, 51.4)



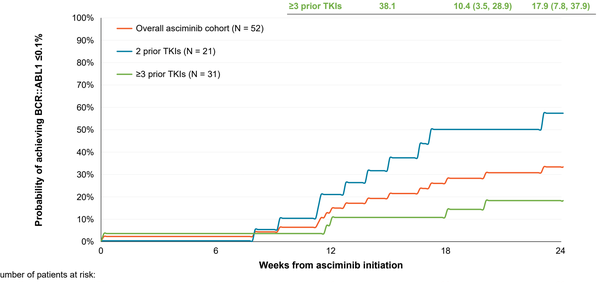
Number of patients at risk:

Overall	70	58	44	38	27
2 prior TKIs	31	26	16	11	6
≥3 prior TKIs	39	32	28	27	21

- As part of a sensitivity analysis, for patients without BCR::ABL1 ≤0.1% prior to asciminib initiation (n=52; **Figure 2c**), 14.6% and 32.9% achieved **BCR::ABL1 ≤0.1%** by 12- and 24-weeks, respectively
  - The median time to BCR::ABL1 ≤0.1% was 30.7 weeks (2 prior TKIs: 23.0 weeks; ≥3 prior TKIs: 38.1 weeks)

Figure 2c. Cumulative incidence of BCR::ABL1 ≤0.1% - sensitivity analysis[1]

	Median time to BCR::ABL1 ≤0.1%, weeks	12-week KM rate (95% CI)	24-week KM rate (95% CI)
Overall	30.7	14.6 (7.2, 28.2)	32.9 (21.2, 48.7)
2 prior TKIs	23.0	20.6 (8.3, 46.0)	56.7 (35.1, 80.3)
≥3 prior TKIs	38.1	10.4 (3.5, 28.9)	17.9 (7.8, 37.9)



Number of patients at risk:

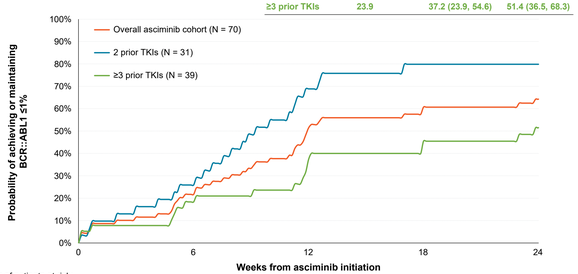
Overall	52	49	40	32	26
2 prior TKIs	21	21	15	8	6
≥3 prior TKIs	31	28	25	24	20

Note:
[1] Patients with BCR::ABL1 ≤0.1% or better in the three months prior to the index date were excluded from this sensitivity analysis.

- In addition, 51.3% (2 prior TKIs: 68.7%; ≥3 prior TKIs: 37.2%) and 64.2% (2 prior TKIs: 79.7%; ≥3 prior TKIs: 51.4%) achieved or maintained **BCR::ABL1 ≤1%** by 12- and 24-weeks, respectively (**Figure 2b**)

Figure 2b. Cumulative incidence of BCR::ABL1 ≤1%

	Median time to BCR::ABL1 ≤1%, weeks	12-week KM rate (95% CI)	24-week KM rate (95% CI)
Overall	12.0	51.3 (40.1, 63.6)	64.2 (52.6, 75.6)
2 prior TKIs	9.3	68.7 (52.1, 84.0)	79.7 (63.6, 92.0)
≥3 prior TKIs	23.9	37.2 (23.9, 54.6)	51.4 (36.5, 68.3)



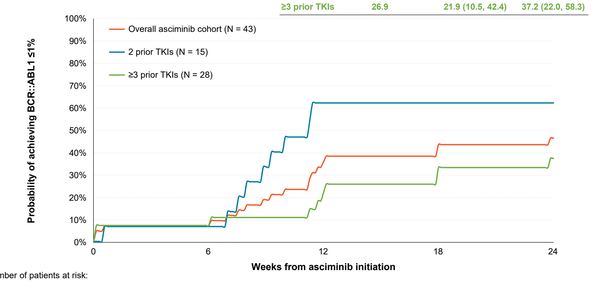
Number of patients at risk:

Overall	70	54	32	28	20
2 prior TKIs	31	23	9	6	4
≥3 prior TKIs	39	31	23	22	16

- Similarly, for patients without BCR::ABL1 ≤1% prior to asciminib initiation (n=43; **Figure 2d**), 35.6% and 46.3% achieved **BCR::ABL1 ≤1%** by 12- and 24-weeks, respectively
  - The median time to BCR::ABL1 ≤1% was 24.6 weeks (2 prior TKIs: 11.3 weeks; ≥3 prior TKIs: 26.9 weeks)

Figure 2d. Cumulative incidence of BCR::ABL1 ≤1% - sensitivity analysis[1]

	Median time to BCR::ABL1 ≤1%, weeks	12-week KM rate (95% CI)	24-week KM rate (95% CI)
Overall	24.6	35.6 (23.2, 52.1)	46.3 (32.4, 62.7)
2 prior TKIs	11.3	61.9 (38.4, 85.4)	61.9 (38.4, 85.4)
≥3 prior TKIs	26.9	21.9 (10.5, 42.4)	37.2 (22.0, 58.3)



Number of patients at risk:

Overall	43	40	26	24	18
2 prior TKIs	15	14	5	4	3
≥3 prior TKIs	28	26	21	20	15

Note:
[1] Patients with BCR::ABL1 ≤1% or better in the three months prior to the index date were excluded from this sensitivity analysis.

LIMITATIONS

- Given included patients with Ph+ CML-CP were largely from community-based oncology practices, the study population may not have been representative of all patients with Ph+ CML-CP in the US
- Assessments of real-world MR may be based on heterogeneous criteria and assessment schedules, and may not be made consistently across included patients

References

1. Jabbour E, et al. *Am J Hematol.* 2022;97(9):1236-1256. **2.** United States Food and Drug Administration. FDA approves asciminib for Philadelphia chromosome-positive chronic myeloid leukemia 2021; https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-asciminib-philadelphia-chromosome-positive-chronic-myeloid-leukemia. **3.** Rea D, et al. *Blood.* 2021;138(21):2031-2041. **4.** Hochhaus A, et al. *Leukemia.* 2023;37(3):617-626. **5.** Ma X, et al. Comparison of population characteristics in real-world clinical oncology databases in the US: Flatiron, SEER, and NPCR; https://www.medrxiv.org/content/10.1101/2020.03.16.20037143v3 **6.** Birnbaum B, et al. Model-assisted cohort selection with bias analysis for generating large-scale cohorts from the EHR for oncology research; https://arxiv.org/abs/2001.09765