Poster # PF597

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Asciminib after One Prior Tyrosine Kinase Inhibitor in Patients with Chronic Myeloid Leukemia – a Physician Panel-Based Chart Review Study in the United States

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KEY FINDINGS & CONCLUSIONS

- In this first and large analysis of real-world treatment patterns and clinical outcomes among US patients with CML-CP who initiated asciminib after one prior TKI, MR rates were high despite inclusion of patients switching to asciminib following treatment failure with a first TKI
- Asciminib was well-tolerated, with nearly all patients remaining on asciminib by 48 weeks post-treatment initiation, supporting the findings of previous clinical trials that have evaluated asciminib as first (i.e., ASC4FIRST trial[4]), second (i.e., ASC2ESCALATE trial[5]), or third or later (i.e., ASCEMBL trial[9]) treatment
- Findings were consistent across subgroups and demonstrated the robustness of rapid and deep treatment responses to asciminib in real-world clinical practice
- Results of the current analysis suggest that asciminib is an effective option for patients previously treated with one prior TKI, regardless of the TKI type and primary reason for discontinuation

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BACKGROUND

- Tyrosine kinase inhibitors (TKIs) are the cornerstone of standard-of-care treatment for patients diagnosed with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia in chronic phase (CML-CP)[1]
- Intolerance and treatment failure with current ATP-competitive TKIs are common in patients with CML-CP[2,3], underscoring the need for treatments with favorable tolerability and efficacy profiles to allow patients to remain on therapy and achieve treatment objectives
- As of October 2024, asciminib, an ABL/BCR::ABL1 TKI targeting the ABL myristoyl pocket, has received US FDA approval for the treatment of adult patients with newly diagnosed or previously treated CML-CP, or CML-CP with the T315I mutation[4,5]
- Since October 2021, asciminib has been indicated for patients with CML-CP previously treated with ≥2 TKIs or with the T315I mutation[6,7]

OBJECTIVE

- Given the lack of real-world evidence, this study aimed to describe clinical outcomes of patients with CML-CP treated with asciminib after one prior TKI in the US clinical practice, providing further insights to the findings from the phase 2 ASC2ESCALATE trial

METHODS

Study design/Data source

- This study was a retrospective physician panel-based chart review study conducted from February to December 2024 using an online case report form completed by hematologists/oncologists from community and academic practices across US census regions
- Retrospective collection of de-identified patient-level data was performed from medical charts of adult patients with CML-CP initiated on asciminib between January 2022 and June 2023 following treatment with one prior TKI
- Institutional review board exemption was obtained from the Pearl IRB

Measures/Outcomes/Statistical analyses

- Time-to-treatment discontinuation (TTD): time from asciminib initiation (index date) until treatment discontinuation (physician assessment; event) or observation period end (censor); evaluated using Kaplan-Meier (KM) analyses
- Reasons for first TKI treatment discontinuation were assessed by physicians; a suggested definition of treatment failure of BCR::ABL1 >10% at 6 months or >1% at 12 months was provided
- Time-to-MR2 (BCR::ABL1 ≤1%)/Time-to-MR3 (BCR::ABL1 ≤0.1%)/Time-to-MR4 (BCR::ABL1 ≤0.01%), separately: time from asciminib initiation until the first MR assessment documenting MR2 or better/MR3 or better/MR4 or better (event) or the earliest occurrence of either treatment discontinuation or observation period end (censor); assessed using KM analyses among patients with MR testing frequency of at least every 3 months
- Subgroup analyses: patients with intolerance to the first TKI, treatment failure to first TKI, and by first- (1G; i.e., imatinib) or second-generation (2G; i.e., bosutinib, dasatinib, or nilotinib) TKI used as first treatment

RESULTS

Physician and patient characteristics

- A total of 76 physicians (**Table 1**) provided data for 255 patients with CML-CP who initiated asciminib after one prior TKI (**Table 2**)

Table 1. Physician characteristics

Physician characteristics	N = 76
Primary practice setting, %	
Community- / Academic-based	47.4% / 52.6%
Urban / Suburban / Rural	65.8% / 28.9% / 5.3%
Primary practice size, %	
Large (≥10 physicians) / Small-intermediate / Individual	71.1% / 26.3% / 2.6%
Primary practice location, %	
Northeast / Midwest / South / West	25.0% / 25.0% / 32.9% /17.1%
Years of practice, %	
<5 / ≥5 to <10 / ≥10 years	0.0% / 14.5% / 85.5%

Abbreviations: N: number

Table 2. Patient characteristics

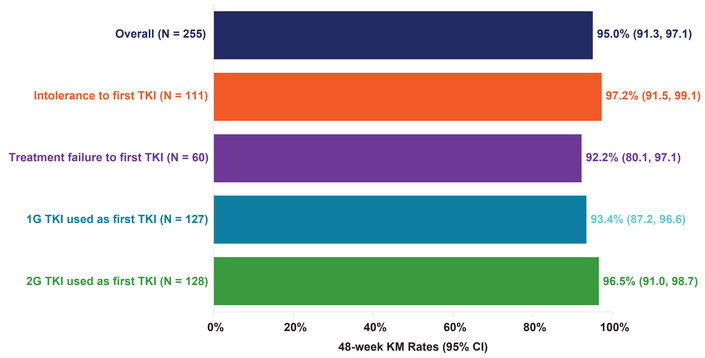
Patient characteristics	N = 255
Median age, years	62.0
Female, %	43.5%
Race/ethnicity, %	
White / Black / Hispanic / Other	56.1% / 20.8% / 16.5% / 6.7%
Sokal score, %	
Low / Intermediate / High risk / Unknown	22.0% / 57.6% / 18.4% / 2.0%
ECOG performance status, %	
Grade 0 / Grade 1 / Grade ≥2	23.1% / 59.6% / 17.3%
First TKI, starting daily dose, n (%)	
Imatinib	127 (49.8%)
<400 mg / 400 mg / >400 mg	0.8% / 89.8% / 9.4%
Dasatinib	88 (34.5%)
<100 mg / 100 mg / >100 mg	5.7% / 76.1% / 18.2%
Nilotinib	27 (10.6%)
<600 mg / 600 mg / >600 mg	48.1% / 33.3% / 18.5%
Bosutinib	13 (5.1%)
<400 mg / 400 mg / >400 mg	0.0% / 100% / 0.0%
Reasons for first TKI discontinuation (top 5), %	
Intolerance	43.5%
Treatment failure	23.5%
Suboptimal response	18.8%
Treatment-free remission	3.9%
Patient preference	3.5%

Abbreviations: ECOG: Eastern Cooperative Oncology Group; mg: milligrams; N: number; TKI: tyrosine kinase inhibitor; US: United States

Treatment patterns

- Median follow-up post-asciminib initiation was 73.6 weeks
- Asciminib was initiated at 40 mg twice daily by 37.6% and 80 mg once daily by 36.9% of patients
- By 48 weeks post-index, 95.0% of patients remained on asciminib (**Figure 1**)
- No patients were observed to progress to accelerated phase or blast crisis post-asciminib initiation
- Constitutional adverse events (AEs) including fatigue (8.6%), headache (7.1%), rash (4.3%) and abdominal pain (2.4%); gastrointestinal AEs including nausea (11.8%), vomiting (6.7%) and diarrhea (4.7%); and cytopenia (2.4%) were observed post-asciminib initiation

Figure 1. Probability of remaining on asciminib by 48 weeks in patients with CML treated with asciminib after one prior TKI[a]

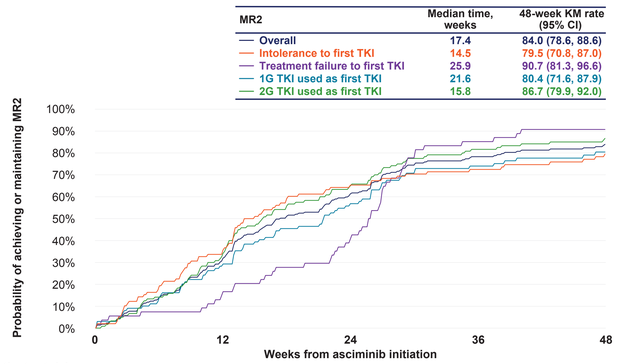


Abbreviations: 1G: first-generation; 2G: second-generation; CI: confidence interval; CML: chronic myeloid leukemia; KM: Kaplan-Meier; TKI: tyrosine kinase inhibitor
Note: [a] Patients remaining at risk at 48-weeks included 182 patients in the overall cohort, 102 in the intolerance to first TKI cohort, 35 in the treatment failure to first TKI cohort, 93 in the 1G TKI as first TKI cohort, and 89 in the 2G TKI as first TKI cohort.

Molecular response

- Cumulative incidence of achieving or maintaining MR2 or better was 84.0% by 48 weeks (**Figure 2**)
- Cumulative incidence of achieving or maintaining MR3 or better was 68.3% by 48 weeks (**Figure 3**)
- Cumulative incidence of achieving or maintaining MR4 or better was 40.6% by 48 weeks (**Figure 4**)

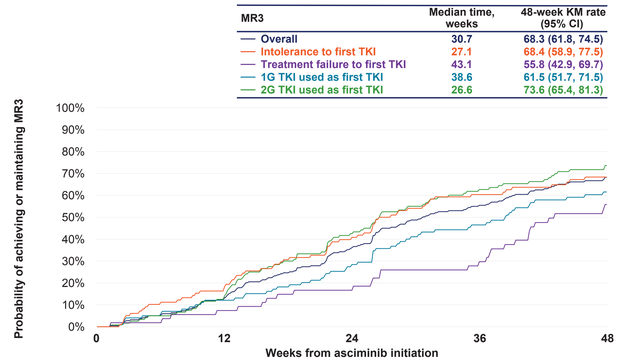
Figure 2. Cumulative incidence of MR2 or better in patients with CML treated with asciminib after one prior TKI



Number of patients at risk:					
Overall	219	152	85	45	31
Intolerance to first TKI	98	65	35	26	18
Treatment failure to first TKI	54	46	33	8	5
1G TKI used as first TKI	99	71	42	23	14
2G TKI used as first TKI	120	81	43	22	17

Abbreviations: 1G: first-generation; 2G: second-generation; CI: confidence interval; CML: chronic myeloid leukemia; KM: Kaplan-Meier; MR: molecular response; TKI: tyrosine kinase inhibitor

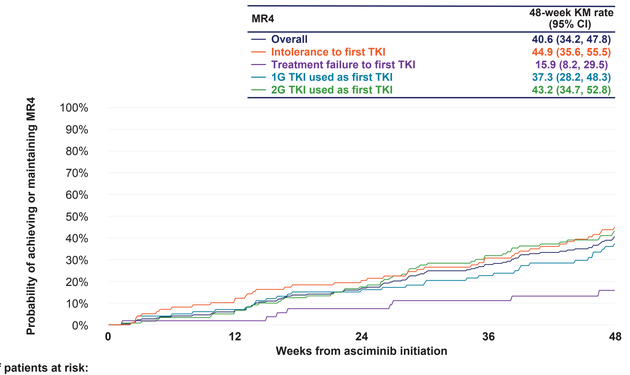
Figure 3. Cumulative incidence of MR3 or better in patients with CML treated with asciminib after one prior TKI



Number of patients at risk:					
Overall	219	192	139	93	60
Intolerance to first TKI	98	82	59	37	27
Treatment failure to first TKI	54	50	45	38	21
1G TKI used as first TKI	99	87	70	49	32
2G TKI used as first TKI	120	105	69	44	28

Abbreviations: 1G: first-generation; 2G: second-generation; CI: confidence interval; CML: chronic myeloid leukemia; KM: Kaplan-Meier; MR: molecular response; TKI: tyrosine kinase inhibitor

Figure 4. Cumulative incidence of MR4 or better in patients with CML treated with asciminib after one prior TKI



Number of patients at risk:					
Overall	219	206	181	149	105
Intolerance to first TKI	98	88	79	66	51
Treatment failure to first TKI	54	53	50	45	31
1G TKI used as first TKI	99	92	82	70	50
2G TKI used as first TKI	120	114	99	79	55

Abbreviations: 1G: first-generation; 2G: second-generation; CI: confidence interval; CML: chronic myeloid leukemia; KM: Kaplan-Meier; MR: molecular response; TKI: tyrosine kinase inhibitor

Limitations

- Findings should be interpreted in the context of the sample selection with unclear generalizability to the overall CML practice in the US
- Assessments of real-world MR may be based on heterogeneous criteria and assessment schedules, and may not be made consistently across patients
- The results may be subject to limitations inherent of retrospective chart reviews, including potential missing data, including AEs, in medical charts

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