Moshe Levy | Moshe.Levy@bswhealth.org

Poster CML-1107

Asciminib Demonstrates Comparable Tolerability and Efficacy With Once-Daily and Twice-Daily Dosing in Chronic Myeloid Leukemia in Chronic Phase: Final Analysis (Week 72) of the Phase 3b AIM4CML Trial

Moshe Levy,[1] David Andorsky,[2] Ghayas Issa,[3] James Essell,[4] Camille Abboud,[5] Andrea Damon,[6] Amy Starinsky,[6] David Coleman,[7] Dheeraj A. Gianchadani,[8] Michael Mauro,[9] Michael Deininger[10]

[1]Baylor Scott & White Health, Dallas, TX, USA; [2]Rocky Mountain Cancer Centers, Boulder, CO, USA; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Oncology Hematology Care, Cincinnati, OH, USA; [5]Washington University School of Medicine, St Louis, MO, USA; [6]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [7]Novartis Pharma AG, Basel, Switzerland; [8]Novartis Healthcare Pvt. Ltd., Salarpuria-Sattva Knowledge City, Hyderabad, India; [9]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [10]The University of Utah, Salt Lake City, UT, USA.

KEY FINDINGS & CONCLUSIONS

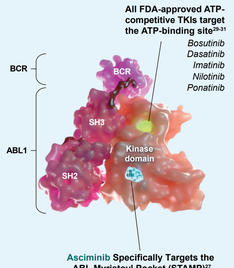
- The end of study analysis of AIM4CML supports the favorable safety, tolerability, and efficacy of both asciminib 40 mg BID and 80 mg QD
  - The safety and tolerability of both doses were comparable and consistent with prior studies of asciminib in this patient population[1-5]
  - No new TEAEs leading to treatment discontinuation occurred between weeks 48 and 72, indicating consistent tolerability across both cohorts
  - By week 72, patients in both cohorts achieved or maintained MMR and/or DMR, which may be prognostic of improved long-term outcomes in CML[6-11]
- Overall, the results from AIM4CML continue to support the flexibility of asciminib QD or BID dosing in patients with CML-CP treated with ≥2 prior TKIs

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INTRODUCTION

- Overall survival and molecular response rates in patients with CML have greatly improved with the advent of TKIs[12-14]; however, a real-world analysis indicated that 26.0% of newly diagnosed patients and 30.5% of patients receiving their second treatment may require treatment switch[15,16]
- Intolerance is among the most common reasons for treatment discontinuation or switch and can lead to nonadherence to treatment[17-20]
- Patients who are nonadherent to their treatment have a lower likelihood of MMR achievement and a higher likelihood of switching TKIs;[21] there remains an unmet need for safe, tolerable therapies with improved efficacy that facilitate long-term treatment
- Asciminib is a *BCR::ABL1* inhibitor that inhibits ABL1 kinase activity by binding to the ABL myristoyl pocket (**Figure 1**)[1]
  - The phase 3 ASCEMBL and phase 1 monotherapy trials led to the approval of asciminib 40 mg BID and 80 mg QD for patients with previously treated Ph+ CML-CP and asciminib 200 mg BID for patients with CML-CP with the T315I mutation[1-3,22,23]
  - The phase 3 ASC4FIRST trial led to the approval of asciminib for patients with newly diagnosed CML-CP[22,24]
- Previously reported exposure-response models have revealed similar efficacy and safety profiles of asciminib 40 mg BID and 80 mg QD in patients without the T315I mutation[25]; furthermore, a more convenient QD dosing regimen may improve patient adherence and outcomes[20]
- In the primary analysis of AIM4CML (NCT04666259), QD and BID dosing of asciminib demonstrated comparable tolerability and efficacy in patients with CML-CP who received ≥2 prior TKIs[26]
- Here we present the EOS (week 72) analysis from the phase 3b AIM4CML trial to further evaluate the safety and efficacy of asciminib monotherapy and QD dosing in patients with CML-CP without the T315I mutation after ≥2 prior TKIs

Figure 1. Asciminib: Designed to Improve Efficacy and Reduce Off-Target Effects vs Current ATP-Competitive TKIs[1,27,28]

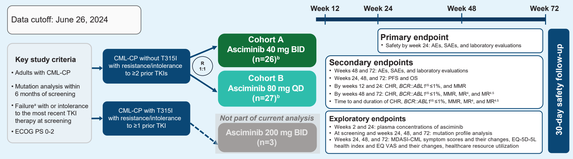


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METHODS

- AIM4CML is a multicenter, phase 3b, open-label study of asciminib in patients with CML-CP without the T315I mutation who have received ≥2 prior TKIs and patients with CML-CP with T315I after ≥1 prior TKI (**Figure 2**)
- Three cohorts were enrolled in the study
  - Cohort A: patients without T315I randomized to receive asciminib 40 mg BID
  - Cohort B: patients without T315I randomized to receive asciminib 80 mg QD
  - Cohort C: patients with T315I assigned to receive asciminib 200 mg BID (not presented in the current analysis)
- The study was not powered to detect statistical differences between cohorts
- The study completion date (last patient last visit) was June 26, 2024
- All patients were followed up for 30 days after the last dose of study treatment for AEs and SAEs during the safety follow-up period
- The primary objective was to evaluate the safety profile of asciminib by week 24 in patients with CML-CP without the T315I mutation after ≥2 prior TKIs[26]

Figure 2. Study Design[26]



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* Must meet failure criteria adapted from the 2020 ELN recommendations.[20] † The study was not powered to detect statistical differences between cohorts.

RESULTS

- At the EOS analysis (week 72), 26 and 27 patients were enrolled in cohorts A and B, respectively
- Baseline characteristics were mostly well balanced between both cohorts; overall, most patients were <65 years old and female (**Table 1**)

Table 1. Demographics and Baseline Characteristics

Characteristic	Cohort A 40 mg BID (n=26)	Cohort B 80 mg QD (n=27)
Age <65 years, n (%)	17 (65.4)	19 (70.4)
Age, median (range), years	58.5 (24.0-81.0)	57.0 (22.0-84.0)
Female, n (%)	16 (61.5)	14 (51.9)
Race, n (%)		
Asian	0	2 (7.4)
Black/African American	4 (15.4)	2 (7.4)
White	21 (80.8)	22 (81.5)
Unknown	1 (3.8)	1 (3.7)
ECOG performance status, n (%)		
0	12 (46.2)	13 (48.1)
1	12 (46.2)	13 (48.1)
2	1 (3.8)	1 (3.7)
Missing	1 (3.8)	0
Time since initial diagnosis, median (range), years[a]	3.3 (0.7-17.6)	5.0 (1.2-17.5)
No. of prior therapies, n (%)		
1	1 (3.8)	0
2	10 (38.5)	13 (48.1)
3	10 (38.5)	10 (37.0)
≥4	5 (19.2)	4 (14.8)

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[a] Time (years) since initial diagnosis of CML = [treatment start date − diagnosis date]/365.25.

- By the EOS data cutoff, 46.2% of patients in cohort A and 74.1% in cohort B completed study treatment (**Table 2**)
  - Overall, 50.0% of patients in cohort A and 25.9% in cohort B discontinued treatment, most commonly because of physician decision due to treatment failure per protocol (15.4% vs 11.1%)
  - The proportion of patients enrolled in safety follow-up was 88.5% in cohort A and 88.9% in cohort B, and the proportion who completed safety follow-up was 76.9% and 85.2%, respectively
  - Discontinuation of safety follow-up was due to treatment failure per protocol, decision based on the protocol, and travel issues (3.8% each) in cohort A and death (3.7%) in cohort B

Table 2. Patient Disposition[a]

Variable, n (%)	Cohort A 40 mg BID (n=26)	Cohort B 80 mg QD (n=27)
Patients treated	25 (96.2)[b]	27 (100)
Patients who completed treatment	12 (46.2)	20 (74.1)
Patients who discontinued treatment	13 (50.0)	7 (25.9)
Primary reason for treatment discontinuation		
Physician decision	9 (34.6)	3 (11.1)
Treatment failure per protocol[c]	4 (15.4)	3 (11.1)
Noncompliance[d]	3 (11.5)	0
Early discontinuation	1 (3.8)	0
Potential future intolerance[e]	1 (3.8)	0
AE	3 (11.5)	1 (3.7)
Patient decision	1 (3.8)	2 (7.4)
Withdrawal of participation	1 (3.8)	0
Patient decided to withdraw	0	1 (3.7)
Patient's co-pay was too high	0	1 (3.7)
Progressive disease	0	1 (3.7)
Patients enrolled in safety follow-up	23 (88.5)	24 (88.9)

[a] By the completion date of June 26, 2024. A total of 3 patients with the T315I mutation were enrolled to receive asciminib 200 mg BID; this treatment arm is not presented in the current analysis. [b] A patient enrolled in cohort A did not receive treatment per patient decision. [c] Includes discontinuation due to treatment failure, treatment failure per protocol, and no MMR. [d] Includes noncompliance and noncompliance while taking prescription.
[e] Investigators provided an explanation of "Discontinuation due to physician decision" at their own discretion.

- The median (range) duration of exposure was 55.3 weeks (2.9-73.3 weeks) in cohort A and 71.0 weeks (1.3-80.6 weeks) in cohort B
- The safety profile of asciminib was similar in cohorts A and B (**Figure 3**)
  - A total of 3 patients (12.0%) in cohort A and 1 (3.7%) in cohort B experienced TEAEs leading to discontinuation, these were neutropenia and thrombocytopenia (in the same patient), abdominal pain, and hypertension (4.0% each) in cohort A and myocardial infarction (3.7%) in cohort B
  - SAEs (any AE [appearance of or worsening of preexisting] undesirable signs, symptoms, or medical conditions that are fatal or life-threatening) were infrequently reported in both cohorts; no fatal SAEs were reported in cohort A, and 1 fatal SAE (3.7%) was reported in cohort B (sepsis)
- AOEs were reported in 2 patients (8.0%) in cohort A and 2 (7.4%) in cohort B
  - In cohort A, brain stem infarction and coronary artery stenosis were reported in 1 patient each
  - In cohort B, acute coronary syndrome, angina pectoris, myocardial infarction, and increased troponin T level were reported in 1 patient, and arteriosclerosis coronary artery was reported in another patient
- No on-treatment deaths were reported in cohort A, and 2 were reported in cohort B (1 each due to study indication/disease progression and sepsis); there were no new on-treatment deaths since the primary analysis
- One patient in cohort B died during the safety follow-up period

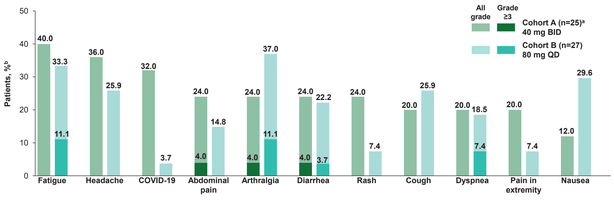
Figure 3. Overview of Treatment-Emergent AEs



[a] One patient in cohort A was assigned to treatment, but treatment was not administered; therefore, the patient was not included in the safety analysis set. [b] A patient with multiple severity grades for an AE is only counted under the maximum grade. [c] All grade. [d] SAEs were defined as any AE (appearance of or worsening of preexisting) undesirable signs, symptoms, or medical conditions that are fatal or life-threatening.

- Similar TEAEs were reported in both cohorts and were mostly grade 1 or 2 (**Figure 4**)
  - In cohorts A and B, respectively, 24 (96.0%) and 26 (96.3%) patients experienced ≥1 TEAE
  - Grade ≥3 TEAEs were reported in 15 patients (60.0%) in cohort A and 14 (51.9%) in cohort B

Figure 4. Most Frequent All-Grade TEAEs (in ≥20% of Patients in Cohort A or B)



[a] One patient in cohort A was assigned to treatment, but treatment was not administered; therefore, the patient was not included in the safety analysis set. * AEs occurring during treatment or within 30 days of the last study medication are presented. A patient with multiple severity grades for an AE is only counted under the maximum grade.

- Dose adjustments and discontinuations occurred in 72.0% of patients in cohort A and 51.9% in cohort B (**Table 3**)
- AEs were the most common reason for adjustments and discontinuations in both cohorts
- No new TEAEs leading to treatment discontinuation were reported between weeks 48 and 72

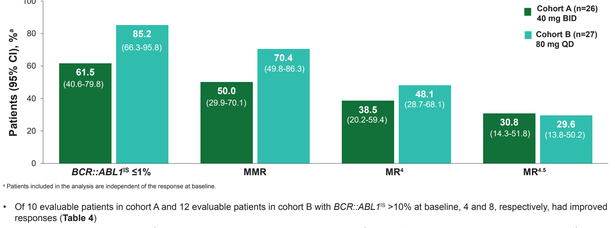
Table 3. Dose Adjustments and Discontinuations

Adjustments and discontinuations/reasons, n (%)[a]	Cohort A 40 mg BID (n=25)[b]	Cohort B 80 mg QD (n=27)
Patients with dose reduction, interruption, or permanent discontinuation	18 (72.0)	14 (51.9)
Reason for dose reduction		
AEs	4 (16.0)	7 (25.9)
Per protocol	1 (4.0)	0
Dispensing error	1 (4.0)	0
Dosing error	0	1 (3.7)
Physician decision	1 (4.0)	0
Reason for dose interruption		
AEs	8 (32.0)	12 (44.4)
Per protocol	2 (8.0)	0
Dosing error	2 (8.0)	2 (7.4)
Physician decision	3 (12.0)	1 (3.7)
Patient decision	1 (4.0)	4 (14.8)
Technical problems	0	1 (3.7)
Reason for permanent discontinuation		
AEs	3 (12.0)	1 (3.7)
Per protocol	0	1 (3.7)
Physician decision	1 (4.0)	0
Patient decision	1 (4.0)	0

[a] A patient with multiple occurrences of a reason for dose reduction or interruption was only counted once in that category. [b] One patient in cohort A was assigned to treatment, but treatment was not administered; therefore, the patient was not included in the safety analysis set.

- By week 72, molecular response rates were comparable between cohorts A and B (**Figure 5**)
- The median time to first MMR was 24.0 weeks (95% CI, 4.1 weeks-NE) in cohort A and 22.9 weeks (95% CI, 11.1-28.3 weeks) in cohort B, and the median time to first MR[4] was 36.1 weeks (95% CI, 11.1 weeks-NE) and 58.6 weeks (95% CI, 23.1 weeks-NE), respectively

Figure 5. Molecular Responses by Week 72



[a] Patients included in the analysis are independent of the response at baseline.

- Of 10 evaluable patients in cohort A and 12 evaluable patients in cohort B with *BCR::ABL1*IS >10% at baseline, 4 and 8, respectively, had improved responses (**Table 4**)
  - Of 10 patients with *BCR::ABL1*IS >10% in cohort A, 2 (20.0%) achieved *BCR::ABL1*IS >1% to ≤10% and 2 (20.0%) achieved *BCR::ABL1*IS >0.1% to ≤1% by 6 months
  - Of 12 patients with *BCR::ABL1*IS >10% in cohort B, 3 (25.0%) achieved *BCR::ABL1*IS >0.1% to ≤1%, 4 (33.3%) achieved *BCR::ABL1*IS >0.01% to ≤0.1%, and 1 (8.3%) achieved *BCR::ABL1*IS ≤0.01% by 6 months

Table 4. Categorical Response Shift From Baseline by 6 Months

Posttreatment *BCR::ABL1*IS	Cohort A 40 mg BID Baseline *BCR::ABL1*IS,a						Cohort B 80 mg QD Baseline *BCR::ABL1*IS,a					
	≤0.01%	>0.01 to ≤0.1%	>0.1 to ≤1%	>1 to ≤10%	>10%	Missing	≤0.01%	>0.01 to ≤0.1%	>0.1 to ≤1%	>1 to ≤10%	>10%	Missing
Evaluable patients	5	2	4	2	10	3	3	4	4	4	12	0
Distribution, n (%)[b,c]												
≤0.01%	5 (100.0)	1 (50.0)	0	1 (50.0)	0	1 (33.3)	2 (66.7)	0	2 (50.0)	1 (25.0)	1 (8.3)	0
>0.01 to ≤0.1%	0	1 (50.0)	2 (50.0)	0	0	0	0	3 (75.0)	1 (25.0)	1 (25.0)	4 (33.3)	0
>0.1 to ≤1%	0	0	2 (50.0)	0	2 (20.0)	0	0	1 (25.0)	1 (25.0)	1 (25.0)	3 (25.0)	0
>1 to ≤10%	0	0	0	1 (50.0)	2 (20.0)	1 (33.3)	0	0	0	0	0	0
>10%	0	0	0	0	5 (50.0)	0	0	0	0	1 (25.0)	2 (16.7)	0
Missing	0	0	0	0	1 (10.0)	1 (33.3)	1 (33.3)	0	0	0	2 (16.7)	0

Compared to baseline, *BCR::ABL1*IS level category: Improved | Did not change | Worsened

[a] The number of patients is the number who received ≥1 dose of asciminib in each category of *BCR::ABL1* transcript level at baseline. [b] Percentages may not total 100 because of rounding. [c] Percentages were calculated on the basis of the number of patients who could be evaluated.

References

1. Rea D, et al. *Blood.* 2021;138:2031-2041.
2. Hochhaus A, et al. *Leukemia.* 2023;37:617-626.
3. Hughes TP, et al. *N Engl J Med.* 2019;381:2315-2326.
4. Mauro MJ et al. *Blood Adv.* Published online May 7, 2025. doi: 10.1182/bloodadvances.2025013444.
5. Réa D, et al. *Leukemia.* 2023;37:1048-1059.
6. Apperley JF, et al. *Leukemia.* 2020;34:1799-1813.
7. Castagnetti F, et al. *Leukemia.* 2015;29:1923-1931.
8. Hanfstein B, et al. *Leukemia.* 2014;28:2443-2448.
9. Jabbour E, et al. *Blood.* 2014;123:494-500.
10. Hehlmann R, et al. *J Clin Oncol.* 2014;32:415-423.
11. Fachi L, et al. *Am J Hematol.* 2013;88:1024-1029.
12. Druker BJ, et al. *N Engl J Med.* 2006;355:2408-2417.
13. Adaikkan JA, et al. *Pharmacol Rev Perspect.* 2022;10:e01005.
14. O'Brien SG, et al. *N Engl J Med.* 2003;348:994-1004.
15. Kota VK, et al. *Blood.* 2020;135(suppl 1):3190.
16. Radich J, et al. *J Med Econ.* 2020;23:761-764.
17. Hahn M, et al. *Am J Manag Care.* 2018;24:e46-54.
18. Claudiani S, et al. *Leukemia.* 2024;38:796-802.
19. Marin D, et al. *J Clin Oncol.* 2010;28:2381-2388.
20. Hochhaus A, et al. *Leukemia.* 2020;34:966-984. 1157-1176.
21. Cheng F, et al. *Int Immunopharmacol.* 2023;124(pt A):110847.
22. Scemblix [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp.
23. Cortes JE et al. *Leukemia.* 2024;38:1522-1533.
24. Hochhaus A, et al. *N Engl J Med.* 2024;391:885-898.
25. Combes FP, et al. *Clin Pharmacokinet.* 2024;63:1301-1312.
26. Levy M, et al. Poster presentation at: SOHO 2024 Annual Meeting; September 4-7, 2024; Houston, TX and virtual. Poster CML-282.
27. Manley PW, et al. *Leuk Res.* 2020;98:106458.
28. Mauro MJ, et al. Oral presentation at: 63rd ASH Annual Meeting & Exposition; December 11-14, 2021; Atlanta, GA. Abstract 310.
29. Deininger M, et al. *Pharmacol Rev.* 2005;57:1-18.
30. Schwartz P, et al. *J Med Chem.* 2018;61:6129-6135.
31. Westerweel PE, et al. *Front Oncol.* 2019;9:665.
32. Andorsky D, et al. *Blood.* 2023;142(suppl 1):3172.

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Abbreviations

ABL1, Abl proto-oncogene 1, non-receptor tyrosine kinase; AE, adverse event; ACE, arterial occlusive event; ATP, adenosine triphosphate; BCR, BCR activator of RhoGEF and GTPase; BID, twice daily; CHR, complete hematologic response; CML, chronic myeloid leukemia; CP, chronic phase; DMR, deep molecular response; ECOG, Eastern Cooperative Oncology Group; EOS, European LeukemiaNet; EQ-5D, EuroQol 5-dimension; EQ VAS, EuroQol visual analog scale; FDA, US Food and Drug Administration; MD/AD-CML, myeloid/lymphoid or acute phase CML; MMR, major molecular response (*BCR::ABL1*IS ≤0.1%); MR4, *BCR::ABL1*IS ≤0.01%; MR4.5, *BCR::ABL1*IS ≤0.0032%; NE, not evaluable; OS, overall survival; PFS, progression-free survival; Ph, Philadelphia chromosome; PR, cytogenetic response; QD, once daily; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TKI, tyrosine kinase inhibitor.

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