Poster CML 398

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Responses with asciminib continue to deepen over time in patients with chronic myeloid leukemia in chronic phase (CML-CP) after ≥2 prior tyrosine kinase inhibitors (TKIs) in the phase 3 ASCEMBL study

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Conclusions

Responses continued to **deepen over time** with **asciminib** in patients with CML-CP previously treated with ≥2 prior TKIs

Patients receiving **asciminib** **achieved *BCR::ABL1*^{IS} ≤1%** and **MMR at week 96** after **resistance** to **all prior 2G TKI therapy**, and **response rates** were **higher** with **asciminib** than with **bosutinib**

A significant portion of patients who continued **asciminib** treatment beyond 6 months (week 24) **could still achieve MMR by later time points** if they had not achieved these responses by week 24

Response rates (MMR and DMR) were **consistently higher** with **asciminib** than **bosutinib** in **most demographic** and **prognostic subgroups**

The efficacy of **asciminib** after treatment failure on 2G TKIs **supports a new standard of care** for patients with **CML-CP** after **≥2 prior TKIs**

This study is sponsored by Novartis Pharmaceuticals Corporation.

For more information, please refer to https://clinicaltrials.gov/ct2/show/NCT03106779.

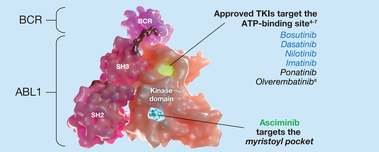
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Introduction

- **Asciminib** is the first BCR::ABL1 inhibitor to **Specifically Target the ABL Myristoyl Pocket (STAMP) (Figure 1)**[1]
- Primary analysis (week 24) results from the pivotal phase 3 ASCEMBL trial helped support **the first approval of asciminib** in the US for patients with **CML-CP previously treated with ≥2 TKIs**[1,2]
- After ≥2 years of follow-up, **asciminib** continued to show **superior efficacy** and **improved safety** and **tolerability** compared with **bosutinib** in patients with CML-CP previously treated with ≥2 ATP-competitive TKIs[3]
- **Asciminib** showed **higher MMR rates** than **bosutinib** at weeks 24 and 96 across major demographic and relevant prognostic subgroups[1,3]
- The number of prior TKIs received, treatment sequence, and reason for discontinuation of the last TKI are known to impact response; all patients in ASCEMBL had received ≥2 prior TKIs, but treatment sequencing and reason for discontinuation of the last TKI varied[1]
- We report **exploratory analyses** from ASCEMBL with the goal of characterizing the efficacy of **asciminib** vs **bosutinib** to investigate **factors associated with response and time to response**

Figure 1. Asciminib Is the First BCR::ABL1 Inhibitor to Specifically Target the ABL Myristoyl Pocket (STAMP)[1]

[a] Approved in China.



Results

- Patients receiving **asciminib** **achieved *BCR::ABL1*^{IS} ≤1% at week 96** after resistance to all prior 2G TKI therapy, and rates were **higher** with **asciminib** than with **bosutinib** (**Table 1**)
  - BCR::ABL1^{IS} ≤1% rates at week 96 were higher in patients with intolerance of at least the last 2G TKI received vs those with resistance to either the last or all lines of 2G TKIs in both treatment arms

Table 1. *BCR::ABL1*^{IS} ≤1% rate at week 96 by the number of prior 2G TKIs received and their reason for discontinuation in patients with *BCR::ABL1*^{IS} >1% at baseline[a]

TKIs received prior to study treatment	Asciminib 40 mg twice daily (n=142)		Bosutinib 500 mg once daily (n=72)	
	n/m[b] (%)	95% CI	n/m[b] (%)	95% CI
2G TKI ± ponatinib ± inv drug ± imatinib	**4/22 (18.2)**	**5.19-40.28**	**3/19 (15.8)**	**3.38-39.58**
2G TKI + imatinib; imatinib as last line	10/14 (71.4)	41.90-91.61	1/5 (20.0)	0.51-71.64
2G TKI ± imatinib; 2G TKI as last line	50/106 (47.2)	37.40-57.11	10/48 (20.8)	10.47-34.99
1 2G TKI[c] ± imatinib	25/53 (47.2)	33.30-61.36	4/17 (23.5)	6.81-49.90
Resistant to all lines of 2G TKIs[d]	14/34 (41.2)	24.65-59.30	2/13 (15.4)	1.92-45.45
Resistant to last 2G TKI[d,e]	0/0	–	0/1 (0.0)	0.00-97.50
Intolerant of last 2G TKI[d,e]	10/18 (55.6)	30.76-78.47	2/3 (66.7)	9.43-99.16
≥2 2G TKIs[c] ± imatinib	25/53 (47.2)	33.30-61.36	6/31 (19.4)	7.45-37.47
Resistant to all lines of 2G TKIs	**10/20 (50.0)**	**27.20-72.80**	**2/12 (16.7)**	**2.09-48.41**
Resistant to last 2G TKI[e,f]	6/17 (35.3)	14.21-61.67	2/10 (20.0)	2.52-55.61
Intolerant of last 2G TKI[e,f]	9/16 (56.3)	29.88-80.25	2/9 (22.2)	2.81-60.01

[a] Based on 142 of 157 patients (90.4%) receiving asciminib and 72 of 76 (94.7%) receiving bosutinib with *BCR::ABL1*^{IS} ≤1% at baseline. [b] n is the number of patients with *BCR::ABL1*^{IS} ≤1% at week 96, and m is the number of patients in the respective subgroup. [c] A patient may have received the same 2G TKI in ≥2 nonconsecutive periods, each constituting a line of 2G TKI therapy. [d] In the asciminib arm, in 1 patient who discontinued their 2G TKI, the reason for discontinuation could not be classified as either resistance or intolerance and is not included in this table. [e] Received in the last line prior to study treatment. [f] Includes a mix of patients with resistance to or intolerance of TKIs received in prior lines.

- Patients receiving **asciminib** **achieved MMR at week 96** after resistance to all prior 2G TKI therapy, and rates were **higher** with **asciminib** than with **bosutinib** (**Table 2**)
  - MMR rates at week 96 were higher in patients with intolerance of at least the last 2G TKI received vs those with resistance to either the last or all lines of 2G TKIs in both treatment arms

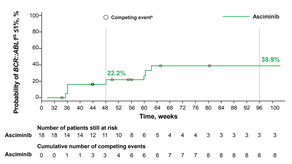
Table 2. MMR rate at week 96 by the number of prior 2G TKIs received and their reason for discontinuation

TKIs received prior to study treatment	Asciminib 40 mg twice daily (n=157)		Bosutinib 500 mg once daily (n=76)	
	n/m[a] (%)	95% CI	n/m[a] (%)	95% CI
2G TKI ± ponatinib ± inv drug ± imatinib	**5/26 (19.2)**	**6.55-39.35**	**2/19 (10.5)**	**1.3-33.14**
2G TKI + imatinib; imatinib as last line	10/15 (66.7)	38.38-88.18	1/6 (16.7)	0.42-64.12
2G TKI ± imatinib; 2G TKI as last line	44/116 (37.9)	29.09-47.41	9/51 (17.7)	8.4-30.87
1 2G TKI[b] ± imatinib	21/56 (37.5)	24.92-51.45	4/19 (21.1)	6.05-45.57
Resistant to all lines of 2G TKIs[c]	12/35 (34.3)	19.13-52.21	1/13 (7.7)	0.19-36.03
Resistant to last 2G TKI[c,d]	0/0	–	0/1 (0.0)	0.00-97.50
Intolerant of last 2G TKI[c,d]	9/19 (47.4)	24.45-71.14	3/5 (60.0)	14.66-94.73
≥2 2G TKIs[b] ± imatinib	23/60 (38.3)	26.07-51.79	5/32 (15.6)	5.28-32.79
Resistant to all lines of 2G TKIs	7/20 (35.0)	15.39-59.22	2/12 (16.7)	2.09-48.41
Resistant to last 2G TKI[c,e]	4/17 (23.5)	6.81-49.90	1/10 (10.0)	0.25-44.50
Intolerant of last 2G TKI[c,e]	12/23 (52.2)	30.59-73.18	2/10 (20.0)	2.52-55.61

[a] n is the number of patients with MMR at week 96, and m is the number of patients in the respective subgroup. [b] A patient may have received the same 2G TKI in ≥2 nonconsecutive periods, each constituting a line of 2G TKI therapy. [c] In the asciminib arm, in 2 patients who discontinued their 2G TKI, the reason for discontinuation could not be classified as either resistance or intolerance and is not included in this table. [d] Received in the last line prior to study treatment. [e] Includes a mix of patients with resistance to or intolerance of TKIs received in prior lines.

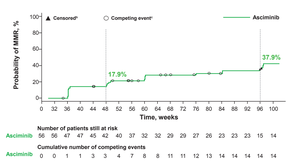
- Among the 18 patients receiving **asciminib** with *BCR::ABL1*^{IS} >1% by week 24 and who remained on asciminib beyond week 24, the probability of ***BCR::ABL1*^{IS} ≤1%** (95% CI) was **22.2% (6.5%-43.6%) by 1 year** and **38.9% (16.4%-61.0%) by 2 years** (**Figure 2**)
- Among the 56 patients receiving **asciminib** with *BCR::ABL1*^{IS} >0.1% (corresponding to a response less than MMR) by week 24 and who remained on **asciminib** beyond week 24, the **cumulative incidence (95% CI) of MMR** was **17.9% (9.1%-29.0%) by 1 year** and **37.9% (25.1%-50.6%) by 2 years** (**Figure 3**)

Figure 2. Cumulative rate of *BCR::ABL1*^{IS} ≤1% among patients with *BCR::ABL1*^{IS} >1% by week 24 and who continued asciminib[a]



[a] Patients with *BCR::ABL1*^{IS} >10% at week 24 discontinued the study and were not included in this analysis. [a] Discontinuation from treatment for any reason without prior achievement of *BCR::ABL1*^{IS} ≤1% is considered a competing event.

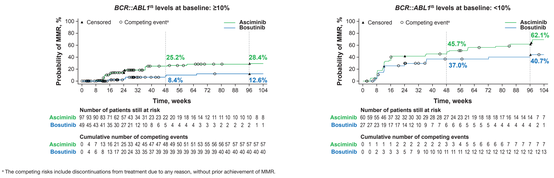
Figure 3. Cumulative MMR rate among patients with *BCR::ABL1*^{IS} >0.1% by week 24 and who continued asciminib[a]



[a] Patients with *BCR::ABL1*^{IS} >10% at week 24 discontinued the study and were not included in this analysis. [a] Nonresponders were censored at their last molecular assessment date. [a] Discontinuation from treatment for any reason without prior achievement of MMR is considered a competing event.

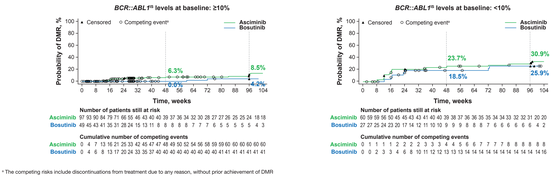
- The **cumulative incidence of MMR** and **DMR** increased in both arms regardless of baseline *BCR::ABL1*^{IS} levels and was **consistently higher** with **asciminib** than with **bosutinib** (**Figures 4** and **5**)

Figure 4. Cumulative incidence of MMR by baseline *BCR::ABL1*^{IS} levels



[a] The competing risks include discontinuations from treatment due to any reason, without prior achievement of MMR.

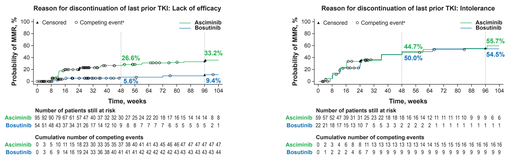
Figure 5. Cumulative incidence of DMR by baseline *BCR::ABL1*^{IS} levels



[a] The competing risks include discontinuations from treatment due to any reason, without prior achievement of DMR

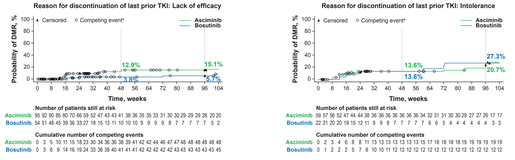
- The **cumulative incidence of MMR** and **DMR** was **consistently higher** with **asciminib** than with **bosutinib** in patients who **discontinued** their **last prior TKI** due to **lack of efficacy** and was **similar** between treatment arms in patients who **discontinued** due to **intolerance** (**Figures 6** and **7**)

Figure 6. Cumulative incidence of MMR by reason for discontinuation of last prior TKI



[a] The competing risks include discontinuations from treatment due to any reason, without prior achievement of MMR.

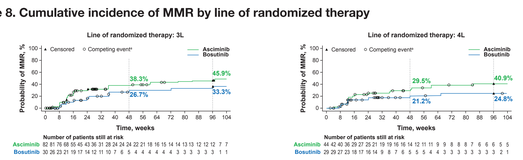
Figure 7. Cumulative incidence of DMR by reason for discontinuation of last prior TKI



[a] The competing risks include discontinuations from treatment due to any reason, without prior achievement of DMR.

- The **cumulative incidence of MMR** increased in both arms regardless of the line of randomized treatment (3L vs 4L) and was **consistently higher** with **asciminib** than with **bosutinib** (**Figure 8**)

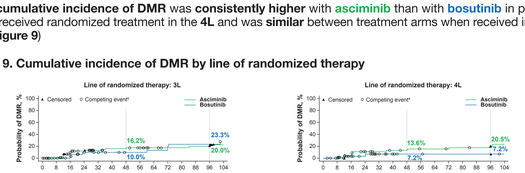
Figure 8. Cumulative incidence of MMR by line of randomized therapy



[a] The competing risks include discontinuations from treatment due to any reason, without prior achievement of MMR.

- The **cumulative incidence of DMR** was **consistently higher** with **asciminib** than with **bosutinib** in patients who received randomized treatment in the **4L** and was **similar** between treatment arms when received in the **3L** (**Figure 9**)

Figure 9. Cumulative incidence of DMR by line of randomized therapy



[a] The competing risks include discontinuations from treatment due to any reason, without prior achievement of DMR.

Abbreviations

2G, second generation; **2L,** second line; **3L,** third line; **4L,** fourth line; **ABL1,** Abelson tyrosine kinase 1; **ATP,** adenosine triphosphate; **BCR,** breakpoint cluster region; **CML-CP,** chronic myeloid leukemia in chronic phase; **DMR,** deep molecular response (MR^5 [*BCR::ABL1*^{IS} ≤0.01%] or better); **inv,** investigational; **IS,** International Scale; **MMR,** major molecular response (*BCR::ABL1*^{IS} ≤0.1%); **SH,** Src homology; **TKI,** tyrosine kinase inhibitor.

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References

1. Rea D, et al. *Blood.* 2021;138(21):2031-2041.
2. Scemblix (asciminib). Prescribing information. Novartis Pharmaceuticals Corp; 2021.
3. Hochhaus A, et al. *Leukemia.* 2023;37(3):617-626.
4. Hochhaus A, et al. *Leukemia.* 2020;34(4):966-984.
5. Schoepfer J, et al. *J Med Chem.* 2018;61(18):8120-8135.
6. Dhillon S. *Drugs.* 2022;82(4):469-475.
7. Westerweel PE, et al. *Front Oncol.* 2019;9:665.