Rapid and Deep Responses With Asciminib in Patients With Chronic Myeloid Leukemia in Chronic Phase After ≥2 Prior Tyrosine Kinase Inhibitors in the Phase 3 ASCEMBL Study

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1South Australian Health and Medical Research Institute and University of Adelaide, Adelaide, Australia; 2Hôpital Saint-Louis, Paris, France; 3Hemorio, Rio de Janeiro, Brazil, and Oncoclínicas, Rio de Janeiro, Brazil; 4National Cancer Center Hospital East, Kashiwa, Japan; 5Memorial Sloan Kettering Cancer Center, New York, NY, USA; 6Georgia Cancer Center at Augusta University, Augusta, GA, USA; 7Centre for Haematology, Imperial College London, London, UK; 8Servicio de Hematología, Hospital Universitario Ramón y Cajal (IRYCS), Madrid, Spain; 9Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; 10Novartis Pharma AG, Basel, Switzerland; 11Novartis Healthcare Private Limited, Hyderabad, India; 12Universitätsklinikum Jena, Jena, Germany
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Introduction

- Asciminib is the first BCR::ABL1 inhibitor to specifically target the ABL Myristoyl Pocket (STAMP)\(^1\).

- 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.

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ABL1, Abelson tyrosine kinase 1; ATP, adenosine triphosphate; BCR, breakpoint cluster region; CML-CP, chronic myeloid leukemia in chronic phase; IS, International Scale; MMR, major molecular response (BCR::ABL1 IS \(\leq 0.1\%\)); SH, Src homology; TKI, tyrosine kinase inhibitor.

\(a\) Approved in China. \(b\) Approved in South Korea.
ASCEMBL Study Design

- **Data cutoff for current analysis:** October 6, 2021
- **Median duration of follow-up:** 2.3 years (120 weeks) from randomization to last contact date
- **Primary endpoint:** MMR rate at week 24
- **Key secondary endpoint:** MMR rate at week 96

**Key study Criteria**

- Adults with CML-CP previously treated with ≥2 TKIs
- Failure\(^a\) or intolerance of most recent TKI
- Patients with intolerance of most recent TKI must have \( BCR::ABL1 \)\(^{1L} \) >0.1% at screening
- No T315I or V299L \( BCR::ABL1 \) mutations

**ASCEMBL** (NCT03106779)

- **Randomized 2:1** (stratified by MCyR vs no MCyR at baseline)
- **N=233**

**Survival follow-up**

**Asciminib**
- 40 mg twice daily
- \( n=157 \)

**Bosutinib**
- 500 mg once daily
- \( n=76 \)

**Treatment duration:** ≥96 weeks

**Switch allowed for those meeting lack-of-efficacy criteria on bosutinib\(^b\)**

\(^a\) Must meet lack-of-efficacy criteria based on 2013 ELN recommendations for 2L TKI therapy. \(^b\) Patients who discontinued bosutinib treatment due to intolerance or any reason other than lack of efficacy were **not** allowed to switch to asciminib.

2L, second line; ELN, European LeukemiaNet; MCyR, major cytogenetic response.
**BCR::ABL1**^IS^ \(\leq 1\%\) 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

<table>
<thead>
<tr>
<th>TKIs received prior to study treatment</th>
<th>Asciminib 40 mg twice daily (n=142)</th>
<th>Bosutinib 500 mg once daily (n=72)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/m^[c] (%)</td>
<td>95% CI</td>
</tr>
<tr>
<td>2G TKI ± ponatinib ± inv drug ± imatinib</td>
<td>4/22 (18.2)</td>
<td>5.19-40.28</td>
</tr>
<tr>
<td>2G TKI + imatinib; imatinib as last line</td>
<td>10/14 (71.4)</td>
<td>41.90-91.61</td>
</tr>
<tr>
<td>2G TKI ± imatinib; 2G TKI as last line</td>
<td>50/106 (47.2)</td>
<td>37.40-57.11</td>
</tr>
<tr>
<td>1 2G TKI^[c] ± imatinib</td>
<td>25/53 (47.2)</td>
<td>33.30-61.36</td>
</tr>
<tr>
<td>Resistant to all lines of 2G TKIs^[c]</td>
<td>14/34 (41.2)</td>
<td>24.65-59.30</td>
</tr>
<tr>
<td>Resistant to last 2G TKI^[d,e]</td>
<td>0/0 –</td>
<td>–</td>
</tr>
<tr>
<td>Intolerant of last 2G TKI^[d,e]</td>
<td>10/18 (55.6)</td>
<td>30.76-78.47</td>
</tr>
<tr>
<td>(\geq 2) 2G TKIs^[c] ± imatinib</td>
<td>25/53 (47.2)</td>
<td>33.30-61.36</td>
</tr>
<tr>
<td>Resistant to all lines of 2G TKIs</td>
<td>10/20 (50.0)</td>
<td>27.20-72.80</td>
</tr>
<tr>
<td>Resistant to last 2G TKI^[e,f]</td>
<td>6/17 (35.3)</td>
<td>14.21-61.67</td>
</tr>
<tr>
<td>Intolerant of last 2G TKI^[e,f]</td>
<td>9/16 (56.3)</td>
<td>29.88-80.25</td>
</tr>
</tbody>
</table>

- Patients receiving **asciminib** achieved **BCR::ABL1**^IS^ \(\leq 1\%\) at week 96 after resistance to all prior 2G TKI therapy, and rates were **higher** with **asciminib** than with **bosutinib**

2G, second generation; inv, investigational.

^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^ \(\leq 1\%\) 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.
MMR Rate at Week 96 by the Number of Prior 2G TKIs Received and the Reason for Discontinuation

<table>
<thead>
<tr>
<th>TKIs received prior to study treatment</th>
<th>Asciminib 40 mg twice daily (n=157)</th>
<th>Bosutinib 500 mg once daily (n=76)</th>
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<tr>
<td></td>
<td>n/m (%) 95% CI</td>
<td>n/m (%) 95% CI</td>
</tr>
<tr>
<td>2G TKI ± ponatinib ± inv drug ± imatinib</td>
<td>5/26 (19.2) 6.55-39.35</td>
<td>2/19 (10.5) 1.3-33.14</td>
</tr>
<tr>
<td>2G TKI + imatinib; imatinib as last line</td>
<td>10/15 (66.7) 38.38-88.18</td>
<td>1/6 (16.7) 0.42-64.12</td>
</tr>
<tr>
<td>2G TKI ± imatinib; 2G TKI as last line</td>
<td>44/116 (37.9) 29.09-47.41</td>
<td>9/51 (17.7) 8.4-30.87</td>
</tr>
<tr>
<td>1 2G TKI ± ± imatinib</td>
<td>21/56 (37.5) 24.92-51.45</td>
<td>4/19 (21.1) 6.05-45.57</td>
</tr>
<tr>
<td>Resistant to all lines of 2G TKIs</td>
<td>12/35 (43.3) 19.13-52.21</td>
<td>1/13 (7.7) 0.19-36.03</td>
</tr>
<tr>
<td>Resistant to last 2G TKI</td>
<td>0/0 –</td>
<td>0/1 (0.0) 0.00-97.50</td>
</tr>
<tr>
<td>Intolerant of last 2G TKI</td>
<td>9/19 (47.4) 24.45-71.14</td>
<td>3/5 (60.0) 14.66-94.73</td>
</tr>
<tr>
<td>≥2 2G TKIs ± ± imatinib</td>
<td>23/60 (38.3) 26.07-51.79</td>
<td>5/32 (15.6) 5.28-32.79</td>
</tr>
<tr>
<td>Resistant to all lines of 2G TKIs</td>
<td>7/20 (35.0) 15.39-59.22</td>
<td>2/12 (16.7) 2.09-48.41</td>
</tr>
<tr>
<td>Resistant to last 2G TKI</td>
<td>4/17 (23.5) 6.81-49.90</td>
<td>1/10 (10.0) 0.25-44.50</td>
</tr>
<tr>
<td>Intolerant of last 2G TKI</td>
<td>12/23 (52.2) 30.59-73.18</td>
<td>2/10 (20.0) 2.52-55.61</td>
</tr>
</tbody>
</table>

• 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

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*a n is the number of patients with MMR at week 96, and m is the number of patients in the respective subgroups. 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.
Cumulative MMR Rate Among Patients With \( BCR::ABL1^{IS} >0.1\% \) by Week 24 and Who Continued Asciminib\(^a\)

- 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

\(^a\) Patients with \( BCR::ABL1^{IS} >10\% \) at week 24 discontinued the study and were not included in this analysis. \(^b\) Nonresponders were censored at their last molecular assessment date. \(^c\) Discontinuation from treatment for any reason without prior achievement of MMR is considered a competing event.
The cumulative incidence of MMR increased in both arms regardless of baseline BCR::ABL1\textsuperscript{IS} levels and was consistently higher with asciminib than with bosutinib.

\textsuperscript{a} The competing risks include discontinuation from treatment due to any reason without prior achievement of MMR.
The cumulative incidence of DMR increased in both arms regardless of baseline \( BCR::ABL^{1\text{IS}} \) levels and was consistently higher with \textbf{asciminib} than with \textbf{bosutinib}.

DMR, deep molecular response (MR4, \( [BCR::ABL^{1\text{IS}}] \leq 0.01\% \) or better).

\(^a\) The competing risks include discontinuation from treatment due to any reason without prior achievement of DMR.
**Cumulative Incidence of MMR by Reason for Discontinuation of Last Prior TKI**

**Reason for Discontinuation of Last Prior TKI: Lack of Efficacy**

- **Asciminib**
  - Probability of MMR, %: 26.6%
  - Time, weeks: 0, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104
  - No. of patients still at risk: 95, 92, 90, 79, 79, 61, 57, 47, 40, 37, 32, 30, 27, 25, 22, 20, 18, 17, 16, 15, 14, 14, 14, 8, 8
  - Cumulative no. of competing events: 0, 3, 5, 10, 11, 15, 18, 23, 30, 33, 35, 36, 36, 38, 40, 41, 41, 41, 42, 42, 42, 42, 43, 43, 43, 43, 43, 43

- **Bosutinib**
  - Probability of MMR, %: 5.6%
  - Time, weeks: 0, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104
  - No. of patients still at risk: 54, 51, 48, 43, 37, 34, 31, 26, 17, 14, 10, 9, 8, 8, 7, 7, 6, 5, 5, 5, 5, 5, 2, 1
  - Cumulative no. of competing events: 0, 3, 6, 9, 14, 16, 19, 24, 33, 36, 36, 38, 40, 41, 41, 41, 42, 42, 42, 42, 43, 43, 43, 43, 43, 44

**Reason for Discontinuation of Last Prior TKI: Intolerance**

- **Asciminib**
  - Probability of MMR, %: 33.2%
  - Time, weeks: 0, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104
  - No. of patients still at risk: 59, 57, 52, 47, 39, 31, 25, 23, 22, 18, 18, 16, 16, 14, 12, 11, 11, 10, 9, 9, 9, 6, 6
  - Cumulative no. of competing events: 0, 2, 3, 4, 6, 8, 8, 11, 13, 13, 13, 13, 13, 13, 13, 14, 14, 15, 15, 15, 16, 16, 16, 16

- **Bosutinib**
  - Probability of MMR, %: 9.4%
  - Time, weeks: 0, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104
  - No. of patients still at risk: 22, 21, 18, 17, 15, 13, 10, 7, 5, 3, 2, 2, 2, 2, 1, 1, 1, 1, 1, 1, 1, 1
  - Cumulative no. of competing events: 0, 1, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2

- The cumulative incidence of MMR 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.

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*The competing risks include discontinuation from treatment due to any reason without prior achievement of MMR.*
Cumulative Incidence of DMR by Reason for Discontinuation of Last Prior TKI

- The cumulative incidence of 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.

\( a \) The competing risks include discontinuation 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.
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.

*a The competing risks include discontinuation from treatment due to any reason without prior achievement of DMR.
Conclusions

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

- Patients receiving **asciminib** achieved $BCR::ABL1^{IS} \leq 1\%$ 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 with **bosutinib** in **most demographic and prognostic subgroups**

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

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References