Efficacy and Safety of Bosutinib by Age and Modified Charlson Comorbidity Index in Previously Treated Patients With Chronic Myeloid Leukemia: Results From the Phase 4 BYOND Study

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Background
- Bosutinib is a tyrosine kinase inhibitor (TKI) approved for the treatment of Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) resistant/intolerant to prior therapy and newly diagnosed Ph+ chronic phase (CP) CML.
- High rates of cytogenetic and molecular responses were observed during treatment with bosutinib 550 mg once daily in the phase 4 BYOND study in patients with Ph+ CP CML who were resistant/intolerant to prior TKIs.
- Increasing age and the presence of comorbidities may influence the outcomes of patients with CML treated with TKIs.

Methods
- BYOND (NCT02288382) is an ongoing, phase 4, single-arm, open-label study examining the safety and efficacy of bosutinib (starting dose 550 mg once daily) in patients with CML resistant/intolerant to prior TKI treatment. Efficacy criteria and endpoints have been previously described.
- Efficacy and safety outcomes are reported in patients with Ph+ CP CML by:
  - Age: ≥65 vs <65 years and ≥75 vs <75 years.
  - Comorbidities assessed by Charlson Comorbidity Index without the age component (mCCI).
- Results were based on 1 year of follow-up (data cut-off date: September 18, 2018).

Results
- A total of 156 patients with Ph+ CP CML received bosutinib (Table 1).
- At the data cutoff, 44.3% vs 62.4% of patients aged ≥65 vs <65 years, 39.3% vs 62.3% of patients aged ≥75 vs ≥75 years, and 62.6% vs 56.0%, and 37.9% of patients with mCCI 2, 3, and ≥4, respectively, were still receiving bosutinib treatment. Reasons for permanent treatment discontinuation are shown in Table 2 and Figure 1.
- A substantial proportion of patients attained or maintained molecular responses across age groups and mCCI groups (Table 1 and Figures 1 and S1).
- No patient experienced on-treatment transformation to accelerated/blast phase CML.
- Grade ≥3 treatment-emergent adverse events (TEAEs) differed between groups; older patients aged ≥65 and ≥75 years and those with mCCI ≥4 had a higher rate of grade 3/4 TEAEs (Figure 2).
- Deaths occurred in 10 out of 96 patients aged ≥65 years old and 4 out of 6 patients aged ≥75 years old. Deaths occurred in 4, 3, and 5 patients with mCCI scores 2, 3, and ≥4, respectively.
- Supplemental material can be accessed via the electronic QR code.

Conclusions
- Examine efficacy and safety of bosutinib by age and comorbidities in patients with Ph+ CP CML resistant/intolerant to prior TKI therapy enrolled in the phase 4 BYOND study.
- Results demonstrate efficacy of bosutinib in patients with Ph+ CP CML resistant/intolerant to prior therapy across age groups and mCCI scores, with a substantial proportion of patients across age and mCCI groups achieving/maintaining molecular response.
- Older patients (aged ≥65 or ≥75 years) and those with high comorbidity burden (mCCI ≥4) showed a trend towards higher rates of TEAEs and were more likely to discontinue treatment due to AEs. Age and mCCI stratification may enable the identification of patients who are at higher risk of developing TEAEs and require more careful monitoring.

Table 1: Background Characteristics in Patients With Ph+ CP CML, by Age and Comorbidities

<table>
<thead>
<tr>
<th>mCCI</th>
<th>&lt;65 (n=95)</th>
<th>≥65 (n=58)</th>
<th>&lt;75 (n=123)</th>
<th>≥75 (n=27)</th>
<th>0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>48 (50.0)</td>
<td>27 (46.6)</td>
<td>75 (60.8)</td>
<td>12 (44.4)</td>
<td>0.75</td>
</tr>
<tr>
<td>3</td>
<td>29 (30.7)</td>
<td>20 (34.5)</td>
<td>47 (38.3)</td>
<td>7 (25.9)</td>
<td>0.24</td>
</tr>
<tr>
<td>≥4</td>
<td>18 (19.0)</td>
<td>11 (19.0)</td>
<td>4 (3.3)</td>
<td>8 (29.6)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Table 2: Treatment Summary in Patients With Ph+ CP CML, by Age and Comorbidities

<table>
<thead>
<tr>
<th>By Age, years</th>
<th>&lt;65 (n=95)</th>
<th>≥65 (n=58)</th>
<th>0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>by comorbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mCCI 2</td>
<td>48 (50.0)</td>
<td>27 (46.6)</td>
<td>0.75</td>
</tr>
<tr>
<td>mCCI 3</td>
<td>29 (30.7)</td>
<td>20 (34.5)</td>
<td>0.24</td>
</tr>
<tr>
<td>mCCI 4</td>
<td>18 (19.0)</td>
<td>11 (19.0)</td>
<td>0.01</td>
</tr>
</tbody>
</table>
| Efficacy and safety outcomes are reported in patients with Ph+ CP CML by age and mCCI groups achieving/maintaining molecular response.

Figure 1: Cumulative MMR Rates in Patients With Ph+ CP CML, by (A) Age and (B) Comorbidities

Figure 2: Summary of Grade 3/4 TEAEs in Patients With Ph+ CP CML, by (A) Age and (B) Comorbidities

References: