Zanubrutinib Safety/Tolerability Profile and Comparison With Ibrutinib Profile in B-Cell Malignancies: Post Hoc Analysis of a Large Clinical Trial Safety Database


INTRODUCTION

- Bruton tyrosine kinase inhibitor (BTK)Is have revolutionized treatment of B-cell malignancies.
- Use of the first-generation BTKIs butritumab may be limited by toxicity—including cardiovascular and gastrointestinal side effects and—sustained to off-target kinase inhibition.
- Zanubrutinib is a selective and potent inhibitor of BTK that has been designed to improve tolerability by maximizing BTK occupancy and minimizing off-target effects.

METHODS

- Clinical trials (N=10) of zanubrutinib monotherapy included in these post hoc safety analyses are shown in Table 1.
- Patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL-SLL), mantle cell lymphoma, marginal zone lymphoma, Waldenström macroglobulinemia, follicular lymphoma, and other B-cell malignancies were included.
- ASPEN (cohort 1) and ALPINE compared zanubrutinib head-to-head with ibrutinib.

RESULTS

- Table 3: Exposure, Dose Adjustments, and Deaths

<table>
<thead>
<tr>
<th>Location</th>
<th>ALL (n=425)</th>
<th>ALL (n=384)</th>
<th>ALL (n=288)</th>
<th>ALL (n=125)</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>409 (96.5)</td>
<td>377 (97.9)</td>
<td>280 (97.9)</td>
<td>114 (90.9)</td>
</tr>
<tr>
<td>Global</td>
<td>17 (4.1)</td>
<td>17 (4.4)</td>
<td>18 (6.3)</td>
<td>11 (8.8)</td>
</tr>
</tbody>
</table>

- Most frequent TEAEs leading to discontinuation were infection events.
- The prevalence of AESIs tended to remain constant or decrease over time with zanubrutinib.
- The prevalence of AESIs tended to decrease over time, without the emergence of new safety signals.
- Due to the consistent dosing of BTKIs in most B-cell malignancies, long-term tolerability and low treatment discontinuation rates with BTKIs are important.

DISCLOSURES

- None.

REFERENCES


ACKNOWLEDGMENTS

- The authors have indicated no financial relationships. This work was supported by BeiGene, Ltd. All authors were required to disclose any potential conflicts of interest in the post hoc analyses presented.