Zanubrutinib vs Ibrutinib in Relapsed/Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma (R/R CLL/SLL): Impact on Health-Related Quality of Life

Barbara Eichhorst,1 Nicole Lamanna,2 Susan M. O'Brien,3 Constantine S. Tam,4 Lugui Ou,5 Keri Yang,6 Ken Wu,7 Tommi Salmi,8 Gisoo Banes,9 Jennifer R. Brown8

1Department of Internal Medicine, University of Cologne, Center for Integrated Oncology, Cologne, Germany; 2Department of Medicine, University College London, London, UK; 3Pathology and Laboratory Medicine, University of Texas Southwestern Medical Center, Dallas, TX; 4Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA; 5Beijing Cancer Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China; 6Sanger Institute, Wellcome Trust Genome Campus, Hinxton, CB10 1SA, UK; 7BeiGene USA, Inc., San Mateo, CA, USA; 8Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, USA

INTRODUCTION

• Symptoms that patients with CLL, including SLL, may experience have a profound negative impact on patients’ health-related quality of life (HRQoL).1,2
• The ALPINE trial (NCT03734019), a randomized, open-label, multi-country phase 3 study, compared zanubrutinib with ibrutinib in patients with R/R CLL/SLL.3 The final progression-free survival (PFS) analysis (August 2022 cutoff date) showed the following:
  • At a median follow-up of 29.6 months, zanubrutinib demonstrated superiority to ibrutinib in overall response rate (86.2% vs 75.1%, nominal P=0.007) and PFS (HR: 0.65 [95% CI, 0.49-0.86]; 2-sided P=0.004).4
• The purpose of the current analyses was to assess HRQoL, as an objective, in patients treated with zanubrutinib or ibrutinib in the ALPINE trial.

METHODS

• The study population consisted of adult patients (aged ≥18 years) that had a confirmed diagnosis of CLL/SLL that met International Workshop on CLL criteria, were R/R to prior systemic therapy, and had an Eastern Cooperative Oncology Group performance status of ≤2.
• Eligible patients were randomized 1:1 to receive zanubrutinib (80 mg oral twice daily, n=327) or ibrutinib (420 mg oral once daily, n=325) until disease progression or unacceptable treatment-related toxicity.

HRQoL Assessments and Endpoints

• Key clinical cycles were cycles 7 and 13.
• Key endpoints from the patient-reported outcomes (PROs) were:
  • The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 (EORTC QLQ-C30); global health status (GH) scale, two functional scales (physical functioning and role functioning), and four symptom scales (fatigue, pain, nausea/vomiting, and diarrhea).
• GHS and functioning scales: higher scores indicate better HRQoL, higher scores on the symptom scales suggest worse HRQoL.
• The EORTC QLQ-ED 5-level questionnaire (EORTC-ED 5L) is a visual analog scale (EQ-VAS) for patients to rate their general health “today.”

Statistical Analyses

• Changes from baseline for each of the key EORTC QLQ-C30 scales and EQ-VAS were analyzed descriptively using means and standard deviations (SD).
• A mixed model for repeated measures (MMRM) compared changes in EORTC QLQ-C30 scores from baseline by treatment group at cycles 7 and 13 – MMRM analyses were conducted only for the key PRO endpoints, in accordance with FDA/EMA requirements, and were selected a priori.
• Clinically meaningful change was defined as a ≥5-point mean difference from baseline.

RESULTS

Patient Demographics and Clinical Characteristics

• The intent-to-treat population consisted of a total of 652 patients (zanubrutinib: 327 patients; ibrutinib: 325 patients).
• Patient demographics and baseline characteristics were comparable in the zanubrutinib and ibrutinib treatment arms (Table 1).
• The observed means and mean change from baseline for the QLQ-C30 are provided in Supplemental Table 1, available for download by scanning the QR code at right.

<table>
<thead>
<tr>
<th>Table 1. Patient Demographics and Disease Characteristics</th>
<th>Zanubrutinib (n=327)</th>
<th>Ibrutinib (n=325)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>67 (35-90)</td>
<td>68 (35-95)</td>
</tr>
<tr>
<td>≥65 years, n (%)</td>
<td>201 (61.5)</td>
<td>200 (61.5)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>213 (65.6)</td>
<td>232 (71.4)</td>
</tr>
<tr>
<td>ECOG PS ≥1, n (%)</td>
<td>196 (60.5)</td>
<td>203 (62.5)</td>
</tr>
<tr>
<td>Prior lines of systemic therapy, median (range)</td>
<td>1 (0-6)</td>
<td>1 (0-6)</td>
</tr>
<tr>
<td>&gt;3 prior lines, n (%)</td>
<td>24 (7.3)</td>
<td>30 (9.2)</td>
</tr>
<tr>
<td>del(17p) and/or ECOG PS ≥1, n (%)</td>
<td>31 (9.5)</td>
<td>32 (9.9)</td>
</tr>
<tr>
<td>Unmutated</td>
<td>233 (71.3)</td>
<td>239 (73.5)</td>
</tr>
<tr>
<td>Complex karyotypen</td>
<td>56 (17.2)</td>
<td>70 (21.5)</td>
</tr>
<tr>
<td>Bulky disease (≥5 cm), n (%)</td>
<td>145 (44.3)</td>
<td>149 (45.8)</td>
</tr>
</tbody>
</table>
• Complex karyotype is defined as having ≥1 abnormality.

Abbreviation: ECOG PS, Eastern Cooperative Oncology Group performance status.

Change From Baseline for EORTC QLQ-C30 in GHS and Functioning Scales

• Both arms improved from baseline to both cycle 7 (Figure 1) and cycle 13 (Figure 2).
• All improvements were clinically meaningful for the zanubrutinib arm; however, by cycle 13, no clinically meaningful differences were observed between the two treatment arms.

Change From Baseline for EORTC QLQ-C30 in Symptom Scales

• Both arms experienced a decrease in fatigue and pain, with the zanubrutinib arm experiencing clinically meaningful improvements in both symptoms at cycle 7 (Figure 3) and cycle 13 (Figure 4).

CONCLUSIONS

• The results of this study suggest that zanubrutinib monotherapy improves HRQoL outcomes in patients with R/R CLL/SLL.
• These improvements were maintained from 6 months through 12 months, the cutoff point for these analyses, suggesting treatment with zanubrutinib positively affected and improved HRQoL over time.
• Given the generally good HRQoL at baseline in both arms, the differences between the arms were not significant.
• Long-term follow-up as well as additional analyses linking PRO endpoints to clinical outcomes will further determine the full extent to which zanubrutinib improves patient HRQoL.

DISCLOSURES

• No funding was received for this study.
• The study was supported by BeiGene, Ltd, and the European Organization for Research and Treatment of Cancer (EORTC).

ACKNOWLEDGMENTS

• The authors would like to thank the investigators and site study personnel for their contributions, global access and support, and the patients, families, and caregivers who participate in clinical trials. The trial was conducted under the auspices of the EORTC and the EORTC Collaborative group.

Figure 1. EORTC QLQ-C30 Mean Change From Baseline in Symptom Scales at Cycle 7 (6 Months) by Treatment

Figure 2. EORTC QLQ-C30 Mean Change From Baseline in GHS and Functioning Scales at Cycle 13 (12 Months) by Treatment

Figure 3. EORTC QLQ-C30 Mean Change From Baseline in Symptom Scales at Cycle 7 (6 Months) by Treatment

Figure 4. EORTC QLQ-C30 Mean Change From Baseline in Symptom Scales at Cycle 13 (12 Months) by Treatment

References

7. Lordick J, Stadler WM, Stuhler G, et al. Median overall survival with ibrutinib compared to 3.92 (16.78) for zanubrutinib and ibrutinib, respectively (16.97) for zanubrutinib and ibrutinib, respectively. 2015
8. The observed mean and mean change from baseline for the QLQ-C30 are provided in Supplemental Table 1, available for download by scanning the QR code at right.