An Improved Benefit-Risk Profile of Duvelisib in Patients With
 Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma
Who Received ≥ 2 Prior Therapies

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BACKGROUND

• Duvelisib (DUV) is a first-in-class, oral dual inhibitor of phosphoinositide 3-kinase δ and ε (PI3Kδ/ε) approved by the US Food and Drug Administration for treatment of relapsed/refractory (RR) chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) in patients who have received ≥ 2 prior therapies1

• DUV targets key signaling pathways that promote the growth and survival of hematologic malignancies.2

• The unique therapeutic potential of dual PI3Kδ/ε inhibition offers a novel approach to treat patients with R/R CLL/SLL.

Figure 1. Duvelisib Dual Inhibitor of PI3Kδ/ε Mechanism of Action

![Duvelisib Mechanism of Action](image)

RESULTS

• Baseline characteristics for those patients who had received ≥ 2 prior therapies (Table 1) were similar to those of the overall DUV population (Table 2).

Table 1. Baseline Characteristics and Prognostic Features

<table>
<thead>
<tr>
<th>Feature</th>
<th>Overall Population (n = 101)</th>
<th>Patients Who Had Received ≥ 2 Prior Therapies (n = 95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, %</td>
<td>82 (81)</td>
<td>90 (94)</td>
</tr>
<tr>
<td>ECOG PS 0/1, %</td>
<td>9 (9)</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Median time from diagnosis to randomization, months</td>
<td>9 (7)</td>
<td>8 (6)</td>
</tr>
<tr>
<td>Rate of ≥ 5/6 grade toxicity, %</td>
<td>20 (20)</td>
<td>20 (20)</td>
</tr>
<tr>
<td>Early discontinuation due to lack of efficacy, %</td>
<td>17 (17)</td>
<td>17 (17)</td>
</tr>
<tr>
<td>Abnormal karyotype, %</td>
<td>16 (16)</td>
<td>16 (16)</td>
</tr>
<tr>
<td>Grade Karyotypic %, median (IQR)</td>
<td>8 (7)</td>
<td>8 (7)</td>
</tr>
</tbody>
</table>

• The ORR or IRC response assessment for DUV was also significantly higher compared with OFA (79% vs 39%; P < .0001) in patients who had received ≥ 2 prior therapies (Figure 3A).

• Among patients who had received ≥ 2 prior therapies, DUV resulted in a lymph node response by IRC assessment of 88% compared with 14% in the OFA arm (P < .001; Figure 3B).

• The only fatal events to occur in > 1 patient were hemorrhagic stroke (n = 2) and pneumonia (n = 2).

• Other causes included sepsis, septic shock, enterococcal sepsis, and bronchopulmonary aspergillosis.

Figure 2. DUO Trial Design

![DUO Trial Design](image)

CONCLUSIONS

• DUV is a first-in-class dual PI3Kδ/ε inhibitor, demonstrated clinical activity with a manageable safety profile in patients with R/R CLL or SLL after ≥ 2 prior therapies.

• Patients who were treated with DUV had 7-month mPFS advantage vs patients who were treated with OFA after ≥ 2 prior therapies.

• DUV decreased the risk of progression in nearly all prespecified high-risk subgroups.

• The majority of heavily pretreated patients responded to DUV (79%, 73% vs 39%; P < .001), with more DUV-treated patients achieving ≥ 50% reduction in target lymph nodes compared with OFA-treated patients (51% vs 14%; P < .001).

• DUV monotherapy represents a new, effective treatment option for heavily pretreated patients with R/R CLL or SLL for whom limited treatment options exist.

REFERENCES


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