Safety and Activity of the Once-Daily Selective Bruton Tyrosine Kinase (BTK) Inhibitor TG-1701 in Patients with Chronic Lymphocytic Leukemia (CLL) and Lymphoma

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BACKGROUND

- BTK inhibition is effective in treating CLL and lymphoma but requires continuous treatment and has potential hepatotoxicity.
- BTK-based combination regimens have the potential to increase depth of response and to permit time-limited frontline therapy.
- TG-1701 is a once-daily (QD) orally available BTK inhibitor that exhibits superior selectivity for BTK with minimal inhibition of other kinases such as Jak3 which have been shown to be associated with off-target effects.

RESULTS

Baseline Characteristics

<table>
<thead>
<tr>
<th>Category</th>
<th>TG-1701 Monotherapy</th>
<th>TG-1701 + U2 Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>72.0 (8.3)</td>
<td>68.9 (10.5)</td>
</tr>
<tr>
<td>Sex, n (% males/females)</td>
<td>7/6</td>
<td>7/6</td>
</tr>
<tr>
<td>Histology</td>
<td>CLL</td>
<td>WM</td>
</tr>
<tr>
<td>- CLL</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>- WM</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>- MCL</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>- SLL</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Prior systemic therapies, median (range)</td>
<td>6 (3–10)</td>
<td>6 (3–10)</td>
</tr>
<tr>
<td>Dose Escalation</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Efficacy

- Median (range) cycles to progression (TP) was 12 (1–23) for CLL patients and 10 (1–14) for WM patients.
- Eight of 10 patients with CLL who received at least one response assessment had progression-free survival (PFS) at least 10 months.

Safety

- No patients had dose-limiting toxicity (DLT) at dose level 3.
- One patient had a dose reduction due to new-onset arthralgias.
- No patients had dose-limiting toxicity at dose level 4.

Pharmacokinetics and Pharmacodynamics

- Peak plasma concentrations were reached within 1 hour of dosing.
- The terminal half-life was 6.4 hours for TG-1701 and 2.0 hours for umbralisib.
- The area under the curve (AUC) was increased at higher doses.

SUMMARY and CONCLUSIONS

- The study results support the continued development of TG-1701 as a QD BTK inhibitor for the treatment of CLL, WM, and MCL.
- Additional studies are needed to further evaluate the efficacy and safety of TG-1701 in these patient populations.