Patients experiencing taladegib

The primary objective of the phase 1b portion of this study was to determine a safe and tolerable dose level of taladegib, and to evaluate the antitumor activity of the combined treatment. Documentation of any antitumor activity of the combined treatment was a secondary objective.

Results

Table 1. Maximum TEASs Possibly Related to Study Drug in 225 Patients

<table>
<thead>
<tr>
<th>Event</th>
<th>Grade 3–4 (%)</th>
<th>Grade 1–2 (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alopecia</td>
<td>3 (15.8)</td>
<td>3 (15.8)</td>
<td>6 (30.8)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>4 (20.0)</td>
<td>1 (5.0)</td>
<td>5 (25.0)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>3 (15.8)</td>
<td>3 (15.8)</td>
<td>6 (30.8)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3 (15.8)</td>
<td>3 (15.8)</td>
<td>6 (30.8)</td>
</tr>
</tbody>
</table>

Table 2. Taladegib and LSN318556 AUCs

Figure 4. GLI Inhibition in Skin by Patient

Although the plasma exposure increased with dose, neither clinical nor laboratory evidence of C/E inhibition was noted upon direct comparison across all doses tested, indicating a robust PD effect.

Conclusions

1. The recommended phase 2 dose for taladegib in combination with C/E is 400 mg daily.
2. The efficacy and pharmacokinetics shown in this combination are comparable to those seen with another Hh/Smoo antagonist given in combination with C/E.
3. The DL of taladegib and LSN18556 are consistent with those observed in a taladegib monotherapy study.
4. GLI inhibition was high across all doses, suggesting robust target engagement in the dose range tested.
5. Due to limited enrollment and the exigence of clinical data from another agent in the same class, the study was discontinued prior to phase 2.

Acknowledgments:

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References: