**BACKGROUND**

- Tilsotolimod (IMO-2125) is an investigational synthetic toll-like receptor 9 (TLR9) agonist with potent immune stimulating activity (Figure 1).

- Preliminary results of a phase 1b study of tilsotolimod plus ipilimumab in solid PD-L1 refractory advanced melanoma demonstrated durable responses and evidence of long-lasting effect.

- **ILLUMINATE-101** (NCT03522200) is a phase 2 study that further explores the role of single-agent tilsotolimod in enrolled patients with stage IV melanoma.

**METHODS**

- Adults with a histologically or cytologically confirmed diagnosis of metastatic melanoma were eligible.

- Patients were randomized 1:1:1 into 3 dose cohorts (n = 15 each; 45 total) to receive daily subcutaneous tilsotolimod 8 mg on 21 days per cycle for a maximum of 10 cycles (Figure 2).

- 8 patients in a cohort experienced DLTs, enrollment of all dose levels was stopped pending cohort review committee recommendations on further study conduct.

- An additional 8 patients were enrolled at the recommended phase 2 dose (6 mg).

**RESULTS**

- Table 1: Demographics and Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N = 54</th>
<th>Mean (SD)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&gt;65 years)</td>
<td>11 (20)</td>
<td>63.0 (11.6)</td>
<td>72</td>
</tr>
<tr>
<td>ECOG PS ≤1 (%)</td>
<td>54 (100)</td>
<td>67.0 (11.6)</td>
<td>72</td>
</tr>
<tr>
<td>HLA-DR (MHC Class II) expression (%)</td>
<td>54 (100)</td>
<td>67.0 (11.6)</td>
<td>72</td>
</tr>
<tr>
<td>Prior treatment (%)</td>
<td>54 (100)</td>
<td>67.0 (11.6)</td>
<td>72</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>54 (100)</td>
<td>67.0 (11.6)</td>
<td>72</td>
</tr>
<tr>
<td>Targeted therapy</td>
<td>54 (100)</td>
<td>67.0 (11.6)</td>
<td>72</td>
</tr>
<tr>
<td>Auto-ADCC (anti-CD47 ADCC)</td>
<td>54 (100)</td>
<td>67.0 (11.6)</td>
<td>72</td>
</tr>
<tr>
<td>Other</td>
<td>54 (100)</td>
<td>67.0 (11.6)</td>
<td>72</td>
</tr>
</tbody>
</table>

**CONCLUSIONS**

- Intratumoral injection of single-agent tilsotolimod was well tolerated and showed promising evidence of clinical activity across multiple solid tumors, including those traditionally unresponsive to immunotherapy.

- Tilsotolimod induced changes in immune checkpoint gene expression in injected tumors, and rapidly increased dendritic cell activation, upregulation of PD-1/PD-L1 signaling, and upregulation of T cell signaling, supporting improved antigen presentation.

- Tilsotolimod-induced upregulation of antigen presentation appears to be similar across tumor types, changes were observed across all tumor types tested, and were consistent with changes observed in a previous phase II clinical trial of patients with metastatic melanoma.

- A phase 2 study of tilsotolimod plus pembrolizumab will be initiated for the treatment of solid tumors (ILLUMINATE-206; NCT03866802).

**REFERENCES**


**DISCLOSURES**

[Author disclosures are included in the paper.]

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