CDX-1140, a Phase 1 dose-escalation/expansion study of CDX-1140 alone (Part 1) and in combination with pembrolizumab (Part 3).

**Baseliner Patient Characteristics**

- **Cohort 1**: Includes patients of both immunoregulatory and allergic responses.
- **Cohort 2**: Patients with advanced tumors who have progressed on standard of care treatment.
- **Part 2**: Combines cohorts of dose escalation and expansion with patients treated at 1.5 mg/kg.

**Pharmacokinetics and Pharmacodynamics**

- **Pharmacodynamics**:
  - Non-kinetic analysis from 3 patients with prostate cancer at 1.5 mg/kg (n=1) and 3 mg/kg (n=2).
- **Immune Modulation in the Tumor Microenvironment**
  - Scores:
    - PBMC isolated from CDX-301 pretreated patients are more responsive to CDX-1140 than PBMC from non-pretreated patients.
  - First demonstration in patients of biological activity within the TME for systemically administered agonist anti-CD40 mAb.

**Clinical Activity for Patients in Part 1 and Part 2 at 1.5 mg/kg**

- Complete metabolic response in a patient with follicular lymphoma.
- Tumor category of follicular lymphoma (Follicular-grade 3 [Flt3L]), pembrolizumab, and cetuximab/unknown.
- Complete metabolic response in a patient with follicular lymphoma.
- Tumor category of follicular lymphoma (Follicular-grade 3 [Flt3L]), pembrolizumab, and cetuximab/unknown.

**Modulation of Immune Pathways**

- Heat map generated by calculating mean difference of pathway scores from all paired biopsies.
- Interferon and cytokine/chemokine pathways were the most highly upregulated.

**Table 1: Baseline Characteristics**

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Part 1</th>
<th>Part 2</th>
<th>Part 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45</td>
<td>48</td>
<td>42</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>Race</td>
<td>White</td>
<td>White</td>
<td>White</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25</td>
<td>26</td>
<td>27</td>
</tr>
<tr>
<td>Prior Rx</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Prior Rx (best response)</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

**Table 2: Treatment-Related AEs of CDX-1140 at 1.5 mg/kg**

<table>
<thead>
<tr>
<th>AE</th>
<th>Part 1</th>
<th>Part 2</th>
<th>Part 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea (n=4)</td>
<td>16</td>
<td>13</td>
<td>17</td>
</tr>
<tr>
<td>Skin rash (n=2)</td>
<td>16</td>
<td>13</td>
<td>17</td>
</tr>
</tbody>
</table>

**Figure 1: Flow cytometric analysis of PBMC at day 0**

- PreRX OnRX.
- Modulation of immune pathways.
- PBMC isolated from CDX-301 pretreated patients are more responsive to CDX-1140 than PBMC from non-pretreated patients.
- First demonstration in patients of biological activity within the TME for systemically administered agonist anti-CD40 mAb.

**Figure 2: Immune cell adhesion and migration**

- Immune cell adhesion and migration pathways were the most highly upregulated.

**Figure 3: Impact of CDX-1140 Pretreatment on PD-1**

- Complete metabolic response in a patient with follicular lymphoma.
- Tumor category of follicular lymphoma (Follicular-grade 3 [Flt3L]), pembrolizumab, and cetuximab/unknown.

**Figure 4: Immune cell activation**

- Complete metabolic response in a patient with follicular lymphoma.
- Tumor category of follicular lymphoma (Follicular-grade 3 [Flt3L]), pembrolizumab, and cetuximab/unknown.

**Figure 5: Modulation of immune pathways**

- Heat map generated by calculating mean difference of pathway scores from all paired biopsies.
- Interferon and cytokine/chemokine pathways were the most highly upregulated.

**Figure 6: Clinical activity for patients in Part 1 and Part 2 at 1.5 mg/kg**

- Complete metabolic response in a patient with follicular lymphoma.
- Tumor category of follicular lymphoma (Follicular-grade 3 [Flt3L]), pembrolizumab, and cetuximab/unknown.

**Figure 7: Baseline Scan**

- Complete metabolic response in a patient with follicular lymphoma.
- Tumor category of follicular lymphoma (Follicular-grade 3 [Flt3L]), pembrolizumab, and cetuximab/unknown.

**Figure 8: On study PET scan**

- Complete metabolic response in a patient with follicular lymphoma.
- Tumor category of follicular lymphoma (Follicular-grade 3 [Flt3L]), pembrolizumab, and cetuximab/unknown.

**Figure 9: On study scan**

- Complete metabolic response in a patient with follicular lymphoma.
- Tumor category of follicular lymphoma (Follicular-grade 3 [Flt3L]), pembrolizumab, and cetuximab/unknown.

**Table 3: Best Overall Response – Response Evaluable Population**

<table>
<thead>
<tr>
<th>Response</th>
<th>Part 1</th>
<th>Part 2</th>
<th>Part 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete metabolic response</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Partial response</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Stable disease</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 4: Summary and future directions**

- CDX-1140 at the recommended dose of 1.5 mg/kg provides good systemic exposure that enhances the distribution into tissues and tumor.
- Tumor category of follicular lymphoma (Follicular-grade 3 [Flt3L]), pembrolizumab, and cetuximab/unknown.
- Correlation between increased expression of PD-L1 and increased clinical activity.
- Correlation between increased expression of PD-L1 and increased clinical activity.