A Phase 1 Trial of a Novel Vaccine Targeting NY-ESO-1 to the Dendritic Cell Receptor DEC-205 in Combination with Toll-like Receptor Agonists

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BACKGROUND

CDX-1401: A Recombinant mAb-NY-ESO-1 Fusion Protein

- NY-ESO-1 is a cancer-testis antigen associated with a number of cancers and validated as tumor rejection antigen.1
- CDX-1401 binds directly to DEC-205 on dendritic cells and stimulates NY-ESO-1 specific CD4 and CD8 responses in preclinical models.2
- Combination with TLR agonists enhances immunity to NY-ESO-1.3

PHASE I CLINICAL STUDY

Open-Label, Dose-Escalation Study of CDX-1401

- Population: Patients with malignancies known to express NY-ESO-1, progressive after available curative/salvage therapies.
- Objectives: Safety, Dose selection, Immune response, Anti-tumor activity

IMMUNE RESPONSE: CDX-1401 TREATED STUDY PATIENTS

Treatment Schema

- CDX-1401 (i.c.)
- Resiquimod (topical or s.c.)
- Poly-ICLC

NY-ESO-1 Tissue Analysis

- Results considered positive if NY-ESO-1 expression detected by either PCR (at any intensity) or IHC (≥5% of cells, ≥1+ intensity). Strongly positive defined as expression by IHC in ≥30% of cells.

Enrolled Patients

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>n</th>
<th>Positive by Either IHC or PCR</th>
<th>Positive by Both IHC and PCR</th>
<th>Strongly Positive by IHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma</td>
<td>57</td>
<td>19 (33%)</td>
<td>15 (26%)</td>
<td>10 (18%)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>38</td>
<td>13 (34%)</td>
<td>4 (11%)</td>
<td>6 (16%)</td>
</tr>
<tr>
<td>Lung</td>
<td>38</td>
<td>9 (24%)</td>
<td>4 (11%)</td>
<td>8 (21%)</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>37</td>
<td>17 (46%)</td>
<td>15 (41%)</td>
<td>14 (38%)</td>
</tr>
<tr>
<td>Ovarian</td>
<td>24</td>
<td>6 (25%)</td>
<td>2 (8%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Breast</td>
<td>15</td>
<td>1 (7%)</td>
<td>1 (7%)</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Bladder/Urothelial</td>
<td>13</td>
<td>3 (23%)</td>
<td>1 (8%)</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Other</td>
<td>59</td>
<td>12 (20%)</td>
<td>1 (2%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>All</td>
<td>281</td>
<td>80 (28%)</td>
<td>43 (15%)</td>
<td>43 (15%)</td>
</tr>
</tbody>
</table>

Safety

- No dose-limiting toxicity (DLT) or discontinuation of treatment due to toxicity.
- Treatment-related toxicities, all Grade 1-2, included administration site reaction (78%), fatigue (24%), nausea (9%) and chills (9%).

Clinical Outcome

- 41 patients completed at least one cycle
- 10 patients were retreated (median [range] = 10 [6 to 20] CDX-1401 doses)
- 13 patients had stable disease (median [range] = 6.7 [2.4 to 13.4] months)
- 7 had melanoma, 2 had colorectal cancer, and 4 had other tumor types
- 4 patients (3 melanoma/1 cholangiocarcinoma) had tumor shrinkage (2, -2, -20 & -21%)
- 8 patients completed study follow-up at 2 years, while an additional 8 remain in follow up.

REFERENCES: