A phase 1 trial of CUE-101, a novel HPV16 E7-pHLA-IL2-Fc fusion protein, alone and in combination with pembrolizumab in metastatic/recurrent HPV+ head and neck cancer


Human papillomavirus (HPV) associated cancers present a significant unmet medical need. Immuno-STATsTM (relative to non-targeted forms of immunotherapy that induce systemic activation of the immune system).

Selective engagement and expansion of tumor antigen-specific T cells also harbors the potential for anticancer efficacy with reduced toxicity.

Prior Lines of Therapy*

<table>
<thead>
<tr>
<th>Category</th>
<th>Patients</th>
<th>N</th>
<th>N = 43</th>
</tr>
</thead>
<tbody>
<tr>
<td>1L</td>
<td>34 (79.1%)</td>
<td>34</td>
<td>34</td>
</tr>
<tr>
<td>2L</td>
<td>25 (58.1%)</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>3L</td>
<td>2 (4.7%)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>≥4L</td>
<td>6 (13.9%)</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

*Data extracted from EDC 31-Oct-2021. Forty-three of 43 patients have demographics and prior therapy data entered in EDC at time of data extract.

Summary

- As of 31-Oct-2021, 44 patients have received CUE-101 monotherapy. Doses ranging from 0.18 to 20 mg/kg were determined to be safe and well-tolerated. Six patients have been administered CUE-101 in combination with pembrolizumab across 2 dose escalations with no DLTs.

- Preliminary PK data demonstrate dose-dependent increase in drug exposure which are sustained upon repeat dosing, with low inter-patient variability. Preliminary clinical laboratory data show early evidence of expansion of HPV16 E7+ T cells. An MTD was not established. Based on the totality of safety, PK, PD, and preliminary anti-tumor activity, Cohort 6 (4 mg/kg) was chosen for RP2D expansion.

- Safety data reported herein were received by CUE Biopharma thru 20-Oct-2021. AEIs were reported generally mild and resolved.

- CUE-101 is a novel agent that is demonstrating acceptable tolerability, favorable PK, and preliminary pharmacodynamic signals that support selective activation of tumor-specific, HPV16+ T cells. One patient has experienced a PR with an ongoing duration of 30 weeks and another 5 patients have experienced SD, defined as stable disease on at least 2 consecutive post-treatment scans through an event.

Methods

- CUE-101 is a novel agent that is demonstrating acceptable tolerability, favorable PK, and preliminary pharmacodynamic signals that support selective activation of tumor-specific, HPV16+ T cells. One patient has experienced a PR with an ongoing duration of 30 weeks and another 5 patients have experienced SD, defined as stable disease on at least 2 consecutive post-treatment scans through an event.

- **Background**

  - Human papillomavirus (HPV)-associated cancers present a significant unmet medical need. Immuno-STATsTM (relative to non-targeted forms of immunotherapy that induce systemic activation of the immune system).

  - Selective engagement and expansion of tumor antigen-specific T cells also harbors the potential for anticancer efficacy with reduced toxicity.

- **Patients and Methods**

  - **CUE-101** is a novel agent that is demonstrating acceptable tolerability, favorable PK, and preliminary pharmacodynamic signals that support selective activation of tumor-specific, HPV16+ T cells. One patient has experienced a PR with an ongoing duration of 30 weeks and another 5 patients have experienced SD, defined as stable disease on at least 2 consecutive post-treatment scans through an event.

- **Safety**

  - Safety data reported herein were received by CUE Biopharma thru 20-Oct-2021. AEIs were reported generally mild and resolved.

- **CUE-101** is a novel agent that is demonstrating acceptable tolerability, favorable PK, and preliminary pharmacodynamic signals that support selective activation of tumor-specific, HPV16+ T cells. One patient has experienced a PR with an ongoing duration of 30 weeks and another 5 patients have experienced SD, defined as stable disease on at least 2 consecutive post-treatment scans through an event.

- **Preliminary Tumor Responses for CUE-101 Monotherapy at the RP2D (4 mg/kg)**

  - **A.** Change from baseline in the sum of target tumor lesions measured by RECIST 1.1 in all patients in Parts A and B treated at the RP2D of 4 mg/kg. **B.** PD-L1 IHC staining on FFPE sections from a representative lesion from a patient with a confirmed partial response at 3 months.

- **Parts B and D: Pembrolizumab and Planned Dose Expansion**

  - **Part B: Expansion to total of 20 patients at RP2D**

  - **Part D: Combination**

- **Low Inter-Patient Variability and Sustained Exposure with Repeat Dosing at the RP2D (4 mg/kg)**

  - **A.** Change from baseline in the sum of target tumor lesions measured by RECIST 1.1 in all patients in Parts A and B treated at the RP2D of 4 mg/kg. **B.** PD-L1 IHC staining on FFPE sections from a representative lesion from a patient with a confirmed partial response at 3 months.

- **Parts C and D: CUE-101 Dose Escalation in Combination with Pembrolizumab and Planned Dose Expansion**

  - **C.** Change from baseline in the sum of target tumor lesions measured by RECIST 1.1 in all patients in Parts A and B treated at the RP2D of 4 mg/kg. **D.** PD-L1 IHC staining on FFPE sections from a representative lesion from a patient with a confirmed partial response at 3 months.

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