Intralesional administration of CovaX213 (CVA21) oncolytic virus immunotherapy in patients with advanced melanoma induces durable tumour responses

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CovaX213 (CVA21: CAuUMAk™) is a naturally occurring “common cold” intercellular adhesion molecule-1 (ICAM-1) targeted RNA virus. Surface ICAM-1 is up-regulated on a number of cancers, including melanoma, non-small cell lung, bladder, breast and prostate cancers. CAuUMAk™ is a novel bio-selected formulation of CVA21, which displays potent oncolytic activity against a wide variety of human cancer cells and in vivo xenografts of a number of cancers. In addition, in vivo tumour challenge studies in immune-competent mouse models have shown that CVA21 lysed tumour cells can induce a secondary systemic host-generated anti-tumour immune response.

Introduction

**Patient Characteristics**

<table>
<thead>
<tr>
<th>Age</th>
<th>Median (range)</th>
<th>94%</th>
<th>75%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECOG status</td>
<td>0</td>
<td>62%</td>
<td>42%</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>58</td>
<td>62%</td>
</tr>
<tr>
<td>Race</td>
<td>Caucasian</td>
<td>56</td>
<td>58%</td>
</tr>
<tr>
<td>Stage at screening</td>
<td>BC</td>
<td>22</td>
<td>25%</td>
</tr>
<tr>
<td>Lung</td>
<td>0</td>
<td>14</td>
<td>16%</td>
</tr>
<tr>
<td>Liver</td>
<td>0</td>
<td>8</td>
<td>13%</td>
</tr>
<tr>
<td>Liver</td>
<td>0</td>
<td>9</td>
<td>21%</td>
</tr>
</tbody>
</table>

**Safety and Tolerance**

- Injection site erythema
- Headache
- Chills
- Pyrexia
- Injection site pain
- Injection site swelling
- Nausea
- Influenza-like illness
- Dysphagia
- Dysphonia
- Rash

**Adverse Events (Alliette)**

<table>
<thead>
<tr>
<th>Grade 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>14 (9%)</td>
</tr>
<tr>
<td>36 (26%)</td>
</tr>
<tr>
<td>75 (52%)</td>
</tr>
</tbody>
</table>

**Grade 2**

- Injection site pain
- Rash

**Grade 3**

- Injection site pain
- Rash

**Grade 4**

- Injection site pain
- Rash

**Grade 5**

- Injection site pain
- Rash

**Adverse Events (CAvatak)**

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**Grade 2**

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**Grade 3**

- Injection site pain
- Rash

**Grade 4**

- Injection site pain
- Rash

**Grade 5**

- Injection site pain
- Rash

**Primary endpoint**

- Best Percentage changes in Target lesions
- Best Percentage changes in non-injected target lung and liver lesions

**Secondary endpoints**

- Patterns of progression
- Median time to response
- Duration of response
- Median survival
- Kaplan-Meier survival
- Median overall survival

**Adverse Events**

- Injection site pain
- Rash

**Adverse Events (CAvatak)**

- Injection site pain
- Rash

**Conclusions**

- The CAvatak trial achieved its primary endpoint with 22/37 pts (60%) IRFS at 6 months.
- Responses were observed in injected lesions, non-injected non-lesions, and in detailed non-responding visceral lesions.
- Multi-cycle intravenous therapy with CVA21 was generally well tolerated (No Grade 3 or 4 treatment related AEs).

**Future Directions**

- The observation of CVA21 induced immune cell infiltrates in human skin suggests that this new approach to cancer immunotherapy may offer significant improvements in the treatment of cancer.
- Clinical evaluation of the activity of intravenous injection of CAvatak in combination with systemic administration of checkpoint inhibitors in patients with metastatic melanoma is currently ongoing (Phase II MTD study, ClinicalTrials.gov identifier NCT02207175) (see Poster P211/2).
- Further evaluations of both intratumoral and intravenous administration of CVA21 in combination with additional immune checkpoint inhibitors are planned.