Introduction

The treatment of non-muscle invasive bladder cancer (NMIBC) has not changed significantly in 25 years. Treatment with intravesical BCG (bacillus Calmette Guerin), or chemotherapy after transurethral resection of tumor (TURBT) does not alter the natural history of the disease and has significant toxicity for patients. CVA21™ (Colloidal Vesicular Assembler 21), is a novel intravesical adjuvant against PD-L1 P and ICAM-1, which is an intercellular adhesion molecule-1 (ICAM-1)-targeted immunotherapeutic virus. Surface ICAM-1 is up-regulated on a number of cancers including melanoma, non-small cell lung, prostate and bladder. Clinical trials of NMIBC cancer patients. CVA21™ (Colloidal Vesicular Assembler 21) treatment of non-muscle invasive bladder cancer (NMIBC) has not changed significantly in 25 years. Treatment with intravesical BCG (bacillus Calmette Guerin), or chemotherapy after transurethral resection of tumor (TURBT) does not alter the natural history of the disease and has significant toxicity for patients.

Study Design

Table 1: Patients and treatment Characteristics

<table>
<thead>
<tr>
<th>Age Group</th>
<th>No. of Patients</th>
<th>Gender M/F</th>
<th>Pathology Finding at TUR</th>
<th>Study Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65</td>
<td>35</td>
<td>20/15</td>
<td>20/15</td>
<td>10-21</td>
</tr>
<tr>
<td>65-79</td>
<td>15</td>
<td>9/6</td>
<td>9/6</td>
<td>10-21</td>
</tr>
<tr>
<td>80+</td>
<td>5</td>
<td>3/2</td>
<td>3/2</td>
<td>10-21</td>
</tr>
</tbody>
</table>

- G1 pTa transitional cell carcinoma
- G2 pTa high grade papillary transitional cell carcinoma
- G3 pTa low grade papillary transitional cell carcinoma

Table 2: Product-related Adverse events

<table>
<thead>
<tr>
<th>Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. RR</td>
<td>30</td>
<td>20</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>2. RA</td>
<td>20</td>
<td>15</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>3. RV</td>
<td>15</td>
<td>10</td>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

Findings 1.

A significant increase in Log TCID2000 was observed in patients treated with CVA21 (Figure 4) compared with untreated NMIBC controls (Figure 4).

Findings 2.

A significant increase in Log TCID2000 was observed in patients treated with CVA21 (Figure 4) compared with untreated NMIBC controls (Figure 4).

Findings 3.

A significant increase in Log TCID2000 was observed in patients treated with CVA21 (Figure 4) compared with untreated NMIBC controls (Figure 4).

Findings 4.

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Findings 5.

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Findings 6.

A significant increase in Log TCID2000 was observed in patients treated with CVA21 (Figure 4) compared with untreated NMIBC controls (Figure 4).

Findings 7.

A significant increase in Log TCID2000 was observed in patients treated with CVA21 (Figure 4) compared with untreated NMIBC controls (Figure 4).

Conclusions

- Proof of concept viral targeting, replication and tumor cell death following a single intravesical administration of CVA21 was achieved in patients with NMIBC. Patients treated with CVA21 had a significant increase in Log TCID2000 compared with untreated NMIBC controls (Figure 4).
- Single agent CVA21 treatment and CVA21 combination treatment were well tolerated with reduced viral doses in combination with intravesical BCG and limited viral load at Day 21 post treatment (Figure 4).
- No evidence of viral spread of CVA21 or development of CVA21 neutralizing antibodies.