TG01/GM-CSF and ADJUVANT GEMCITABINE IN PATIENTS WITH RESECTED RAS-MUTANT ADENOCARCINOMA OF THE PANCREAS

Svein Dustland1, Juan W. Valle2, Katinka Bell3, Zhousha Fu4, Helen Stalger5, Trine Gjertsen6, Anne-Sophie Mallier7, Anne-Kristal Aksnes1, Daniel H. Palmer1

1 University of Liverpool Cancer Research UK Centre, Liverpool, United Kingdom; 2The Norwegian Radium Hospital and Oslo University Hospital, Oslo, Norway; 3Institute of Cancer Sciences, University of Manchester, The Christie NHS Foundation Trust, Manchester, United Kingdom; 4Targovax ASA, Oslo, Norway

BACKGROUND

TG01 is the first subcutaneous cancer immunotherapy (CSIT) targeted to people with RAS-mutation positive tumors. TG01 consists of a recombinant human cytotoxic T-lymphocyte antigen 4 (CTLA-4) fusion protein. The adjuvant gemcitabine (GM-CSF) drives cell growth and maturation and is found in more than 80% of pancreatic adenocarcinoma tumors.

TG01 induces RAS mutant specific T-cell responses which are enhanced by GM-CSF and are necessary to sustain the CD8+ cytotoxic T-cell effect1,8,9. TG01 induces RAS mutant-specific T-cell responses which are enhanced by TG01 specific T-cells which is necessary to sustain the CD8+ cytotoxic T-cell effect10. There is scope for improvement in adjuvant treatment of resected pancreatic cancer; 7-codons in the nucleotide sequence of codon 12 and 13 are the most common codon 12 and 13 oncogenic mutations in TG01 specific T-cells after stimulation with TG01 compared to unstimulated cells. 48 hours after injection has an average diameter

RESULTS

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Number of patients (N=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>KRAS mutation detected</td>
<td>13 (68%)</td>
</tr>
<tr>
<td>M stage</td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>7 (37%)</td>
</tr>
<tr>
<td>N1</td>
<td>12 (63%)</td>
</tr>
<tr>
<td>T stage</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>T3</td>
<td>17 (90%)</td>
</tr>
</tbody>
</table>

Table 2. Immune response by week 11 and through the entire study (n=19)

<table>
<thead>
<tr>
<th>Time</th>
<th>Immune response by week 11</th>
<th>Immune response through entire study</th>
</tr>
</thead>
<tbody>
<tr>
<td>w1</td>
<td>16/19 (84%)</td>
<td>18/19 (95%)</td>
</tr>
<tr>
<td>w2</td>
<td>16/19 (84%)</td>
<td>18/19 (95%)</td>
</tr>
<tr>
<td>w3</td>
<td>10/19 (53%)</td>
<td>14/19 (74%)</td>
</tr>
<tr>
<td>w4</td>
<td>10/19 (53%)</td>
<td>14/19 (74%)</td>
</tr>
</tbody>
</table>

Figure 3 gives an overview of all 19 patients showing their immune response by week TG01 patients, 80% are alive in the study period (n=18/19 patients). 6 patients were still alive when last patient completed the 2 years visit which is also shown in the figure. The high % positive immune responses show that the T-cell vaccination requires antecedent several cycles of gemcitabine and resolved within 1–2 hrs. The high % positive immune responses show that the TG01 vaccination requires antecedent several cycles of gemcitabine and resolved within 1–2 hrs.

Figure 6 shows DSS and OS for all patients.

Table 3. Serious Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bloodstream infection</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Urosepsis</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Anaphylactic reaction</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Anaphylactic shock</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Anaphylactic shock related to a concomitant infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperglycaemia</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Respiratory disorders</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Sensory and neurological disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular disorders</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Skin and appendage disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunological and multorgan related disorders</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CONCLUSIONS

The regimen was generally well tolerated although some late, noticeable adverse

REFERENCES


Targovax

www.targovax.com