An open label phase I study of ABR-217620, a fusion protein of the 5T4 antibody moiety and an engineered superantigen, in patients with non-small cell lung, renal or pancreatic cancer

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**INTRODUCTION**

ABR-217620 (maturemab celladenov) is a recombinant fusion protein that consists of an anti-STF Fab moiety genetically fused to the engineered superantigen variant SEAE-120. This fusion protein is a 2nd generation tumor targeted superantigen based on the previously described ABR-214936 (anatomol makulon). ABR-217620 has reduced antiguity and toxicity in preclinical studies. The ST4 antigen is expressed on more than 95% of tumors from patients with non-small cell lung (NSCLC), renal cell (RCC) and pancreatic cancer (PC). In clinical PET studies its labeled ABR-217620 has been shown to localize to 5T4 positive tumors.

**RESULTS**

**Patient Characteristics**

<table>
<thead>
<tr>
<th>Disease</th>
<th>No. of Patients</th>
<th>Median Age (Years)</th>
<th>Sex (M:F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSCLC</td>
<td>19</td>
<td>39-61</td>
<td>1M:5F</td>
</tr>
<tr>
<td>RCC</td>
<td>8.75</td>
<td>37-61</td>
<td>6M:5F</td>
</tr>
<tr>
<td>PC</td>
<td>4.92</td>
<td>39-69</td>
<td>1M:5F</td>
</tr>
</tbody>
</table>

**Safety**

35 patients have been treated (19 NSCLC, 10 RCC, 6 PC). 5 patients had DLT at doses between 20 and 28 µg/kg/day. Based on the experience with ABR-214936, these side effects were expected, but the MTD of ABR-217620 is ~ 200 times higher. The side effects resolved quickly.

**Primary Endpoint**

Determine the MTD of ABR-217620 as a function of pre-treatment anti-SEA/E-120 levels in patients with advanced non-small cell lung cancer, renal clear cell carcinoma or pancreatic cancer.

**Secondary Endpoints**

Determine the safety profile, pharmacokinetic parameters of ABR-217620, immunological response to the treatment, objective tumor response, time to progression and survival.

**Immunogenicity**

Anti-SEA/E-120 before and 28 days after first dose (median increase in anti-SEA/E-120 titres in approximately 60% of the patients. HAMA levels were generally low.

**Immunology**

Cytokines

ABR-217620 infusion leads to a dose dependent systemic increase of cytokines including IL-2 and IFN-γ.

**Selective T cell expansion**

ABR-217620 treatment leads to expansion of the T cells; approximately 5% of all T cells). The results are presented as a quantitative ratio of TCR-β DNA copies and HPRT (hypoxanthine-guanine phosphoribosyltransferase; house-keeping gene) DNA copies. Samples from 6 patients treated at doses around 20 µg/kg were analyzed.

**CONCLUSION**

ABR-217620 treatment had predicted manageable side effects with fever, hypotension, liver toxicity and nausea being dose limiting toxicities. Treatment with ABR-217620 resulted in a restricted systemic activation of the immune system. Formal efficacy data can obviously not be concluded, but will be evaluated in phase II trials in RCC and NSCLC as combination with docetaxel. The phase I study is still ongoing to refine the estimated MTD.