A first-in-human dose escalation study of PEGylated recombinant human IL-10 (AM0010) in advanced solid tumors.

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AM0010 - BACKGROUND

AM0010 is a pegylated recombinant form of human IL-10 (PEG-IL-10) that is being developed for the treatment of cancer.

Intra-tumoral injection of IL-10 can result in survival in cancer patients.

Immune checkpoint inhibitors increase the number of CD8+ T cells in the tumor.

AM0010-mediated antitumor responses depend upon pretreatment activation by CD8 T cells.

PEG-IL-10 increases intra-tumoral CD8+ T cells and activates them through STAT3 signaling.

In preclinical studies, PEG-IL-10 induces the reactivation of large tumors and the development of immunological memory against the tumor cells.

Figure 1. AM0010 Activates Intra-tumoral CD8+ T cells

Dosing and Toxicity

23 patients (Table 2) in dose escalating cohorts of 3-45 mg/kg were enrolled at doses of 2.5, 5, 10, 20 and 40 mg/kg.

No identification of a Maximum Tolerated Dose (MTD).

2.5 mg/kg: pegylation density was lower than AM0010 (in vivo).

No dose-limiting toxicities (DLT) were identified in the cohort.

2 patients had DLT defined related to AM0010: grade 3 esophageal cancer and grade 3 enteritis.

Other uncommon events include: pruritus, rash, and eosinophilia.

AM0010 PK

AM0010 exposure was clearly dose-proportional at levels of 0.1–29 mg/kg over 28 days (see Figure 8).

RESULTS

Table: Patient Characteristics

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Prior Therapies</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCC</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Melanoma</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Colorectal</td>
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<td>5</td>
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</table>

CONCLUSIONS

The authors would like to acknowledge the patients and their families participating in this clinical trial.

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CONTACT INFORMATION

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