**BACKGROUND**

Intratumoral (IT) injection of *Clostridium novyi-NT* (C. novyi-NT), an attenuated strain of Clostridium, induced a macroscopically precise, tumor-localized response in a rat orthotopic brain tumor model and in companion dogs bearing spontaneous solid tumors.1

In rats, *C. novyi-NT* spores injected into implanted glioma tumors resulted in a significant survival advantage. Brain edema was a common toxicity and was able to be managed medically.1

In companion dogs, *C. novyi-NT* spores injected into single solid tumors resulted in a response rate (CR or PR) of 37.5% (6/16 dogs). The most common toxicities were expected and associated with bacterial infection. These included tumor inflammation, abscess, and pain.1

Additionally, preclinical studies have shown that *C. novyi-NT* injection can induce a systemic anti-tumor immune response.2

**METHODS**

**Endpoints**

- To determine the maximum tolerated dose (MTD), and dose-limiting toxicities (DLT) of a single intratumoral injection of *C. novyi-NT* using the standard 3+3 dose escalation schedule
- To document preliminary anti-tumor activity of both the injected tumor and an overall response
- To study the disposition of circulating *C. novyi-NT* spores
- To measure the host immune and inflammatory response to *C. novyi-NT* administered as a single IT injection in humans with treatment-refractory solid tumor malignancies

**Major eligibility criteria**

- Adult patients with advanced refractory cancers
- Target tumor that is amenable to percutaneous injection of *C. novyi-NT* spores
- ECOG 0-2
- ANC ≥ 1,000/uL
- Hemoglobin ≥ 9 g/dL
- Platelets ≥ 100,000/uL
- Total bilirubin ≤ 1.5 uL upper limit of normal (ULN)
- ALT/AST ≤ 2.5 x ULN
- INR ≤ 1.3
- No primary brain malignancies or brain metastases
- No active infection or treatment with antibiotics

**RESULTS**

### Dose Escalation

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>Dose of Intratumoral C. novyi-NT Spores</th>
<th>Number of patients</th>
<th>Dose-limiting toxicities (DLT)</th>
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<tbody>
<tr>
<td>1</td>
<td>1 x 10⁶</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>5 x 10⁶</td>
<td>3</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>10 x 10⁶</td>
<td></td>
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<tr>
<td>4</td>
<td>30 x 10⁶</td>
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</tr>
<tr>
<td>5</td>
<td>100 x 10⁶</td>
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</tr>
</tbody>
</table>

**Patients Characteristics (n=6)**

- Median age – years (range): 63.5 (39-68)
- Male/Female: 2/4
- Median prior therapies (range): 6.5 (4-9)
- Cancer types:
  - Leimyosarcoma: 2 (34%)
  - Chondrosarcoma: 1 (17%)
  - Carcinosarcoma: 1 (17%)
  - Angiosarcoma: 1 (17%)
  - Papillary thyroid cancer: 1 (17%)

**Inflammation and Immune Markers**

CRP and IL6 showed significant increases in this patient that were coincident with the changes observed on CT and MRI.

**毒理数据摘要**

**CONCLUSIONS**

- Intratumoral injection of *C. novyi-NT* is feasible and has lead to significant destruction of injected tumor masses in the first two doses studied
- Dose escalation is ongoing


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**CFK**

- **CRP and IL6 in Patient 011-001**
- **Baseline:** contrast enhancing mass involving soft tissue and possibly adjacent bone. Lesion measures about 7.2cm AP x 7.4cm transverse in the axial dimensions
- **Day 3:** internal destruction of injected tumor masses
- **Day 4:** markedly diminished contrast enhancement within the tumor mass of soft tissue and possibly adjacent bone component
- **Day 28:** non-enhancing tumor mass becomes more homogeneous consistent with ongoing necrosis