Intravenous Delivery of Toca 511 in Patients With High Grade Glioma Results in Quantifiable Expression of Cytosine Deaminase Protein in Tumor Tissue

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17 17 13 11 9 6 5 2 11 11 0
Baseline 1 1 1 1 1 1 1 1 1 1 1

Best Overall Response – Independent Radiologic Review
- Best response (Macdonald criteria) – stable disease in 3 of 17 patients (17.6%)  
- 2 of 17 patients achieved radiologic responses with delayed onset following clinical progression
  - Anaplastic astrocytoma (IDH1 mt) at 3rd recurrence  
  - Complete response (CR) at 5.9 months after discontinuing Toca FC
  - Patient died (PD) at 14.4 years after initiation of treatment
  - GBM (IDH1 wt) at 2nd recurrence  
  - Complete response (CR) at 10 months after initiation of Toca FC
  - Remains in response of 2 of 17 patients – duration 6+ months
  - Toca FC ongoing; no other anticancer therapy

Toca 511 (Vectamistain amrtrimtropro) is an investigational retroviral replicating vector (RRV) that encodes the transgene cytosine deaminase (CD) not present in human cells. Toca 511 can be delivered by multiple routes and selectively infects and spreads in tumor cells. Subsequent oral administration of investigational extended-release 5-FC (Toca FC) results in formation of 5-FU within infected tumor cells expressing CD. 5-FU kills cancer cells and Myeloid Derived Suppressor Cells (MDSCs) leading to immune activation against the tumor via a combination of mechanisms. This sequence of events is amplified with multiple cycles of Toca FC. Treatment with Toca 511 and Toca FC selectively destroys cancer cells within the body, while leaving healthy cells unharmed.

Introduction and Background

Toca 511 - optimized RRV expressing CO, a drug activator gene

Phase 1 Ascending Dose Trials in rHGG Explored Different Delivery Techniques for Toca 511

Tocagen FC - investigational extended-release oral formulation of 5-FC
- 5-FU crosses blood-brain barrier and is approved for fungal infections of the brain
- CD converts 5-FC to 5-FU within infected cells
- GBM cell lines and MDSCs are sensitive to 5-FU
- 5-FU mediated killing triggers anticancer immunity from within tumor with systemic benefit
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- 5-FU mediated killing triggers anticancer immunity from within tumor with systemic benefit

Clinical Results

Toca 511 & Toca FC – Clinical Development in Primary and Metastatic Brain Tumors

Demographic & Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n = 17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>50.0 years (28-77)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>8 (47.1)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>17 (100)</td>
</tr>
<tr>
<td>KPS, n (%)</td>
<td>70-80 3 (17.6), 90 11 (64.7), 100 3 (17.6)</td>
</tr>
</tbody>
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Neuro-Oncology History

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n = 17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months since initial diagnosis, median (range)</td>
<td>16.8 (6-70)</td>
</tr>
<tr>
<td>Initial tumor histology, n (%)</td>
<td>GBM 14 (82.4)</td>
</tr>
<tr>
<td>Anaplastic astrocytoma</td>
<td>1 (5.9)</td>
</tr>
<tr>
<td>Anaplastic oligodendroglioma</td>
<td>2 (11.8)</td>
</tr>
<tr>
<td>Gross total resection of initial tumor, n (%)</td>
<td>10 (58.8)</td>
</tr>
<tr>
<td>Number of recurrences (including on-study), n (%)</td>
<td>1 (5.8)</td>
</tr>
</tbody>
</table>

Tissue Processing for Analysis of Toca 511

Data point of a given color represent samples from a given patient
- 1 “cytosine deaminase high” sample analyzed/patient
- 1 “cytosine deaminase low” sample analyzed/patient

Tissue Infiltration

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Data cut-off 17 April 2017.

References: