C-REV selectively replicates in tumor cells and breaks them down without damaging to normal cells. When locally injected into a tumor, C-REV shows two different effects as described below.

Direct anti-tumor effects by viral replication. Systemic anti-tumor effects by activated cytotoxic T lymphocytes following tumor destruction.

**INTRODUCTION**

Cancerpancreas (C-REV, formerly HONC is an oncolytic, spontaneous mutant Herpes Simplex Virus type 1, and is one of immunotherapies that combine direct tumor cell killing with immune modulation. This study was designed to determine the recommended dose of C-REV in combination with chemotherapy (Gemcitabine + Nab-paclitaxel). Grade 3 or 4 unresectable pancreatic cancer: the dose escalation in 2 dose levels of C-REV was performed according to the standard 3+3 design.

**METHODS**

**INCLUSIONS/Criteria:**
- Dose Limiting Toxicity (DLT)
- Safety using CTCAE 4.0
- Best overall response rate (BORR) using RECIST 1.1 at Week 16 and study completion
- Progression-free survival (PFS)
- Viral Shedding:
  - White blood cell count decreased transiently.
  - Related with G1-AEs related with C-REV.
- Local r.
- Baseline blood, saliva, urine and faces by qPCR.
- Overall survival (OS), 1 year survival rate

**RESULTS**

**FACIALITY**

**Best Overall Response Rate**

<table>
<thead>
<tr>
<th>Response</th>
<th>N (%)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose level 1</td>
<td>Dose level 2</td>
<td>ALL</td>
</tr>
<tr>
<td>Objective response (CR+PR)</td>
<td>1(16.7%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Complete response (CR)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Partial response (PR)</td>
<td>1 (16.7%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Stable Disease (SD)</td>
<td>2 (33.3%)</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>Progressive Disease (PD)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Not Evaluable (NE)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

**END POINTS**

- Objective response rate (CR + PR): 66.7%
- Progression-free survival at 16 weeks: 83.3%
- Overall survival at 1 year: 33.3%
- Toxicity: Grade 3 acute pancreatitis related to C-REV was detected in one patient.

**SUMMARY OF RESULTS/CONCLUSIONS**

Six patients (pts) were enrolled and treated: 33.3% (2/6) men, age range 63 to 72 y., disease stage III 33.3%, II 66.7%.

**CONCLUSIONS**

The recommended dose was determined as 1x10^5 TCID/mL, but no AEs were reported related with C-REV. Six patients had Grade 3 AEs related with G1-AE, but no AEs were reported related with C-REV. Of the 6 evaluable patients, BORR at 16 week was 33.3% (2/6), BORR at cut off (Oct, 2018) was 16.7% (1/6). Disease control rate was 100% (2/2) and 50%, and 1 of 2 pt continue the study treatment. The samples were collected from 6 pts. HONC virus DNA was not detected by qPCR in any samples of whole blood, saliva, urine and faces except one whole blood sample transiently detected below LLOQ.

**ANALOGNEMENTS**

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Corresponding author: Yusuke Hashimoto, E-mail: yushashi@east.ncc.go.jp