- BO-112 is a GMP preparation of dsRNA (poly I:C) formulated with the cationic carrier polyethylénimine that is capable to trigger both cancer cells and immune cells responses in preclinical cancer models towards immunogenic cell death and increase of immune-checkpoint inhibition effects (fig 1).
- Intratumoral BO-112 alone or combined with systemic anti-PD-1 is being analyzed in this 1st in human clinical trial (NCT02828098).

**METHODS**

- 28 patients with solid tumors and metastases ≥1 cm amenable to injection were enrolled in 4 cohorts (C).
  - C1: single IT BO-112 dose of 0.6 mg (N=6)
  - C2: 1 mg IT BO-112 qw x 2-3 doses (N=7)
  - C3: 0.6 mg IT BO-112 qw x 2-3 doses (N=3)
  - C4: Primary anti PD-1 refractory patients were treated with 1 mg IT BO-112 qw x 2 or 3 doses before continuing nivolumab or pembrolizumab combined with BO-112, until progression, limiting toxicity or up to 1y (N=12).
- BO-112 injected into a single lesion, (if lesion responds, becoming too small, divide dose between original and additional lesion).

**RESULTS: TOXICITY AND PHARMACOKINETICS**

- Frequency of treatment-emergent adverse events of C1-4 are summarized in table 1.
- No safety signals were detected with the combination. BO-112 was not detected in blood.

<table>
<thead>
<tr>
<th>Part 1 – Cohorts 1-3</th>
<th>All TEAEs</th>
<th>Serious TEAEs</th>
<th>Grade 3-5 TEAEs</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>10 (100)</td>
<td>0</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Number of subjects, N = 16 (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1 (40)</td>
<td>0</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Number of events</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**RESULTS: IMMUNOBIOLOGICAL EFFECTS COHORTS 1-3**

- No safety signals were detected with the combination. BO-112 was not detected in blood.

**RESULTS: RECID 1.1 FROM COHORT 4 AND PATIENT EXAMPLE**

- Preliminary disease control rate at 1st assessment (8-12 weeks) was 7/12 (58%) and objective response rate 2/17 (12%), one PR in melanoma and one PR in renal cancer.

**CONCLUSIONS**

- BO-112 has demonstrated a manageable safety profile as single agent and combined with anti-PD-1.
- Its mechanism of action comprises direct antitumor effects and innate and adaptive immune system activation.
- Combination with anti PD-1 is feasible in anti PD-1 refractory patients.
- Preliminary efficacy analysis suggests the potential to halt or reverse primary resistance to anti-PD1 treatment.
- Cohort 4 (BO-112 + anti PD-1 in anti PD-1 refractory patients) is being expanded to include up to 30 patients.