**IMP-MEL: A phase 1 first-in-human dose-finding study of a novel invariant natural killer T-cell agonist (iNKT) IMM60 in advanced melanoma and non-small-cell lung cancer (NSCLC)**

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**BACKGROUND**

- IMM60 (PORT-2) is a synthetic derivative of α-galactosamine formulated into a liposome
- IMM60 is a potent agonist of invariant natural killer T-cells (iNKTs) which leads to activation of the innate and adaptive immune systems, and down regulation of the suppressive tumor microenvironment
- In preclinical studies, IMM60 has demonstrated monotherapy activity in PD-1 resistant models
- IMM60 upregulates PD-L1 expression on cancer cells and may overcome resistance to anti-PD-1 antibody therapy (Figure 1)

**EXPOSURE AND SAFETY**

**Exposure**

- A total of 27 IMM60 infusions have been administered to 6 patients at 1 mg/m² and 3 mg/m² doses, with a median of 4 doses per patient
- The MTD has not been reached

**Safety**

- No SAEs or Dose Limiting Toxicities have been observed
- 5/6 patients (83%) experienced at least 1 AE considered to be related to IMM60; these related AEs were low grade and manageable (Table 2)

**CLINICAL ACTIVITY**

- One patient (3 mg/m²) achieved >50% reduction in a 4 cm mediastinal lesion (Figure 2), and resolution of 2.2 cm lesion in the small bowel mesentery as well as multiple pathologic lymph nodes (the RECIST best response was Stable Disease)

**BLOOD BIOMARKERS**

- Serum cytokine analysis and flow cytometry was analyzed from samples taken prior to treatment and then at 4 hrs, 24hrs and 1 week
- MCP-1 (Figure 3) and IP-10 (Figure 4) showed increases in most subjects, no increases in IL-6, IL-4 and IL-10
- iNKTs downregulate their TCR when the agonist binds to the receptor, indicating activation of the iNKT
- Increase in CD86+ B-cells following treatment with PORT-2

**CONCLUSIONS**

- This trial provides early proof of concept using a small molecule iNKT agonist formulated in a liposome
- Liposomal IMM60 (PORT-2) is well tolerated at 1 and 3 mg/m² with preliminary evidence of clinical activity as a monotherapy
- Serum biomarker analysis provide evidence of iNKT activation, as well as increases in potential surrogate markers of immune response
- Once the Recommended Phase 2 Dose (RP2D) is defined, a multi-national Phase 2 study will be initiated, including 4 arms testing PORT-2 alone or combined with a PD-1 inhibitor

**REFERENCES**


**ACKNOWLEDGMENTS**

We extend our gratitude to the patients, their families, and the University of Oxford site staff members who are making this trial possible.

**STUDY POPULATION**

8 patients have been treated as of Nov 3, 2022, including 1 each in the 9 mg/m² IMM60 monotherapy and 3 mg/m² IMM60 + pembrolizumab combination cohorts.

Data for 6 patients evaluable as of the clinical cutoff date are reported herein.

**METHODS**

- Phase I is a 3+3 design starting with IMM60 monotherapy at doses 1mg, 3mg and 9mg/m²
- IMM60 at 3 and 9mg/m² will also be evaluated in combination with pembrolizumab 200 mg
- IMM60 is administered IV every 3 weeks x 6 cycles
- Patients were evaluated for safety, biopsies and blood were taken before and during treatment

**STUDY DESIGN**

**Figure 1:** IMM60 (PORT-2) Mechanism of Action

**Figure 2:** Clinical Data Snapshot: September 14, 2022

**Figure 3:** Immunocompetent human tumor xenografts (Figure 3).

**Figure 4:** Immunohistochemistry for CD86+ B-cells (Figure 4).

**Figure 5:** IMPORT-201 Study Schema

**Figure 6:** Kaplan-Meier curves for PFS and OS (Figure 6).

**Table 1:** Demographics and Baseline Characteristics (n=6)

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>n=6</th>
<th>3 Melanoma</th>
<th>4 NSCLC</th>
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<tbody>
<tr>
<td>Gender</td>
<td></td>
<td>3 Male</td>
<td>3 Female</td>
</tr>
<tr>
<td>Prior therapies (min/max)</td>
<td>5 (3,7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior PD-1 therapy</td>
<td>100%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Performance status</td>
<td>50% ECOG 0</td>
<td>50% ECOG 1</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2:** Adverse Events related to IMM60 (n=6)

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3-5</th>
</tr>
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<tbody>
<tr>
<td>Dizziness</td>
<td>1 (17%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0</td>
<td>1 (17%)</td>
<td>0</td>
</tr>
<tr>
<td>Flu-like symptoms</td>
<td>1 (17%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hair Loss</td>
<td>1 (17%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (17%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0</td>
<td>1 (17%)</td>
<td>0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (17%)</td>
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</tr>
</tbody>
</table>

**EudraCT Number:** 2020-001351-41

*Clinical Data Snapshot: September 14, 2022*