Preclinical Activity and Manufacturing Feasibility of Genetically Modified PDCD-1 Knockout (KO) Tumor-Infiltrating Lymphocyte (TIL) Cell Therapy

Arvind Natarajan,1 Anand Veerapathran, Adriean Wells,1 Courtney Herman,1 Viktoria Gontcharova,1 Kenneth Onimus,1 Marcus Machin,1 Seth Warelid,1 Jamie L. Blauvelt,2 Madan Jagasia,1 Rafael Cubas3
Tovance Biotherapeutics, San Carlos, CA, USA;1 Moffitt Cancer Center, Tampa, FL

Background

• Although effective, anti–programmed cell death protein (PD)-1 ICI therapy is limited by poor penetration into the tumor.
• TIL have high potency and release of cytokines and other mediators to inhibit tumor growth.
• However, TIL storage and manufacturing are costly, and large-scale expansion is technically challenging.

Results

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Introduction

• Development of IOV-4001, a genetically modified autologous TIL product, was initiated to develop a high potency and effective TIL product.

Methods

• KO TIL were generated using TALEN®-mediated genome editing.
• KO TIL were expanded ex vivo using IL-2 and CD3/CD28 stimulation.

Results

• KO TIL were able to be expanded ex vivo for multiple rounds without losing viability.
• KO TIL showed similar phenotype and function as mock TIL.

Discussion

• KO TIL showed improved efficacy compared to mock TIL.

Conclusions

• KO TIL are a promising new approach for TIL therapy.

Table 1. Summary of Karyotyping Results From PDCD-1 KO TIL Products

<table>
<thead>
<tr>
<th>Sample ID</th>
<th>KO Efficiency</th>
<th>Cytogenetic Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>KO TIL 1</td>
<td>63% (48%–81%)</td>
<td>Normal female: 46a, XXb</td>
</tr>
<tr>
<td>KO TIL 2</td>
<td>70% (50%–80%)</td>
<td>Normal male: 46a, XYb</td>
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References

1. Arvind Natarajan; arvind.natarajan@iovance.com

Acknowledgments

• The authors thank their colleagues for their contributions to this work.

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