**Background**

Cancer, with curative intent, seeks a pathologic invasion that results in altered states of self-tolerance. 

**Primary**

- To evaluate the safety of NEO-PV-01 related to personalized neoantigens 
- To evaluate the safety and immunogenicity of the personalized neoantigen vaccine
- To evaluate the safety of adjuvant

**Secondary**

- To evaluate immune responses at Week 26, assessed by antibody response and cytokine release
- To determine the immune response correlate, defined as immune response categories at Any Time of Death
- To evaluate progression-free survival, overall survival, and duration of response

**Exploratory**

- To evaluate immune response correlates including evaluations of antigen-specific CD4+ and CD8+ T-cell responses to neoantigens
- To correlate patient responses with exploratory parameters, such as programmed death-ligand 1 (PD-L1) expression and tumor mutational burden

**Study Design**

- NEO-PV-01 is a personalized neoantigen vaccine currently designed with up to 20 neoantigen peptides
- The vaccine is composed of up to 20 neoantigen peptides of 14–35 amino acids
- Peptides are pooled together in four groups of up to five peptides each, and mixed
- The peptides are synthesized and pooled together in four groups of approximately 50 mg

**Objectives**

- To achieve complete objective response in at least 10% of patients receiving nivolumab in patients with unresectable or metastatic melanoma, smoking-associated NSCLC, or Transitional Cell Carcinoma of the Bladder

**Study Assessments**

- Safety
- Efficacy
- Immune Profiling and Monitoring
- Study Immunotyping Questions and Key Assays

**Efficacy**

- Investigative assessments to evaluate response to treatment (patient-level, longitudinal evaluation of treatment efficacy in patients with unresectable or metastatic melanoma, smoking-associated NSCLC, or Transitional Cell Carcinoma of the Bladder)

**Table 1. Key Patient Eligibility Criteria**

<table>
<thead>
<tr>
<th>Key Patient Eligibility Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
</tr>
<tr>
<td>Melanoma, Non-Small Cell Lung Carcinoma, or Transitional Cell Carcinoma of the Bladder</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
</tr>
<tr>
<td>Melanoma, Non-Small Cell Lung Carcinoma, or Transitional Cell Carcinoma of the Bladder</td>
</tr>
<tr>
<td><strong>Exploratory</strong></td>
</tr>
<tr>
<td>Melanoma, Non-Small Cell Lung Carcinoma, or Transitional Cell Carcinoma of the Bladder</td>
</tr>
</tbody>
</table>

**Tumor Profiling**

- **DNA & RNA**
- **Bioinformatics**
- **Immune Profiling: Informs and Improves Clinical Feedback Loop**

**Treatment**

- During pre-treatment, patients undergo a baseline tumor biopsy, and collection of peripheral blood
- Human immune antigen typing is performed for each patient
- Mutant neoantigens are designed and RMV expressing plasmids are manufactured based on both the percentage and level of selected targets
- The NEO-PV-01 vaccine is designed based on computational immunomemory analysis of selected targets, which include mutanome, proteome, and transcriptome
- On Day 84 of patients will be randomized (1:1:1) to receive either nivolumab alone or nivolumab in combination with RMV expressing plasmids

**Study Immunotyping Questions and Key Assays**

- ELISPOT, Intracellular cytokine staining
- Melanoma, NSCLC, T-cell receptor

**Figure 5. Immunotyping Questions and Key Assays**

**Figure 4. Treatment and Assessment Schedule**

- **Nivolumab**: 240 mg (first dose) until PD (maximum 2 years)
- **Pemiglatine**: 100 mg (once daily) for 6 weeks

**Study Immunotyping Questions and Key Assays**

- **DNA & RNA**: 80 mL
- **Blood draw**: 80 mL
- **Leukapheresis**: 80 mL
- **Biopsy**: 80 mL

**Figure 5. Immune Monitoring: Informs and Improves**

- LEUKAPHERESIS: Cell processing, leukapheresis
- IMMUNE PROFILING: Informs and improves clinical feedback loop