2021 ESMO congress

Poster ID: 1367 TiP

IMPRINTER: An Open Label, Multi-Center, Dose Escalation/Expansion, Phase 1 Study of IMU-201 (PD1-Vaxx), a B-Cell Immunotherapy, in Adults with Non-Small Cell Lung Cancer

IMUGENE

John Jae Won Park[1], Gary Richardson[2] , Martin Gutierrez[3], David Carbone[4], Michael Boyer[5], Panayiotis Savvides[6], Pravin Kaumaya[7], Tanios Bekaii-Saab[6], Tri Giang Phan[8], Leslie Chong[9], Rita Laeufle[9], Nicholas Ede[9], Bonnie Nlxon[9], Anthony J. Good[9]

[1]Macquarie University Hospital, Sydney, Australia; [2]Cabrini Hospital Malvern, Melbourne, Australia; [3]Hackensack University Medical Center, New Jersey, NY; [4]The James Comprehensive Cancer Center, Columbus, OH; [5]Chris O'Brien Lifehouse Hospital, Sydney, Australia; [6]Mayo Clinic, Phoenix/Scottsdale, AZ; [7]Ohio State University, Columbus, OH; [8]St Vincent's Clinical School, UNSW, Sydney, Australia; [9]Imugene, Sydney, Australia,

Background

Therapies with monoclonal antibodies targeting PD-1 and its ligands are associated with remarkable outcomes in various cancers and, together with antibodies targeting CTLA-4, have revolutionized cancer treatment (Honey 2017). Some patients treated with PD-1/PD-L1 blockade may develop a "primary or secondary resistance" to therapy (Sharma, Hu-Lieskovan et al. 2017). The hypothesis is that a polyclonal induced B-cell antibody response will be more effective or as effective with improved safety over current monoclonal antibody therapy.

IMU-201 is being developed using an active immunization approach to treat cancers that overexpress programmed cell death ligand 1 (PD-L1) by inducing the production of anti-PD-1 antibodies through immunization of patients with a peptide epitope designed to stimulate polyclonal antibodies against PD-1 (Kaumaya et al. 2020).

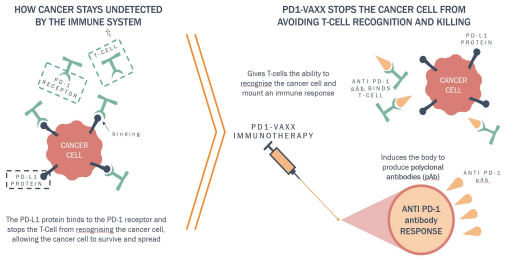


Figure 1, MOA of PD1-Vaxx

Study Description

The IMPRINTER study is an open-label dose escalation/dose expansion study of IMU-201 as monotherapy treatment for PD-L1 expressing lung cancer, to evaluate safety, tolerability, and immunogenicity and assess the optimum biological dose (OBD) of IMU-201 to be used for further clinical development. All patients enrolled in the study must have previously received an immune checkpoint inhibitor for their underlying cancer and experienced disease progression.

The study will continue into combination therapy that includes combination with SOC which may include a monoclonal AB (such as anti-PD-L1)

Study Design

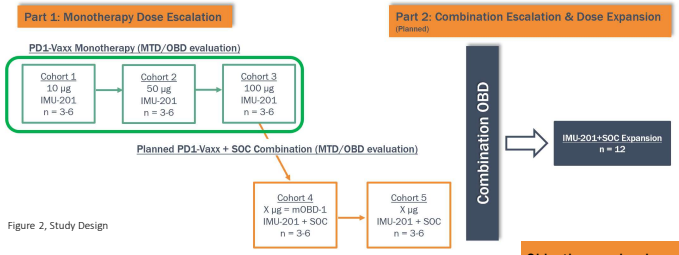
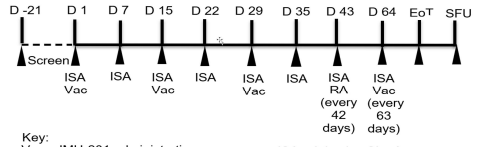


Figure 2, Study Design

Participating Countries and Sites

Figure 3 Map participating countries and sites

Treatment Regimen



Key:
Vac = IMU-201 administration
RA = Radiographic Assessment
SFU = Survival Follow-Up

ISA = Injection Site Assessment
EoT = End of Treatment Visit

Figure 4, Vaccination schedule

Patient Selection

Histologically confirmed non-small-cell lung cancer (NSCLC) tumor stage IIIb or IV (3 major types of NSCLC are acceptable including squamous, adenocarcinoma, and large cell carcinoma);
Progressed on an approved PD-1 inhibitor or an approved PD-L1 inhibitor

Tumor PD-L1 overexpression with Tumor Proportion Score (TPS) ≥ 50%. Patients with PD-L1 TPS ≥ 1% expression may be included with agreement of Imugene Limited;

Objectives and primary Enpoints

Primary Objectives

- To evaluate safety/tolerability and immunogenicity of IMU-201 as monotherapy following treatment with PD-1 inhibitor or PD-L1 inhibitor therapy in patients with advanced NSCLC tumors that are positive for PD-L1.
- To identify the Optimal Biological Dose (OBD) of IMU-201 as monotherapy (mOBD), in patients with advanced NSCLC tumors that are positive for PD-L1.

Secondary Objectives

- To evaluate the efficacy of IMU-201 as monotherapy following treatment with SOC including monoclonal PD-1 inhibitor or PD-L1 inhibitor therapy in patients with advanced NSCLC tumors that are positive for PD-L1.

Exploratory Objectives

To evaluate changes in immunological, biomarker and additional radiological markers of tumor progression in patients treated with IMU-201 as monotherapy.

Primary Endpoints:

- Frequency of patients experiencing adverse events (AEs) graded by Common Terminology Criteria for Adverse Events (CTCAE) v5.0.
- Frequency of patients discontinuing study treatment due to AEs.
- The OBD of IMU-201 evaluated by safety/tolerability and immunogenicity data (IMU-201 and PD-1 specific antibody (IgG) titers).

Study Status

The study has fully enrolled into the third dose cohort, each cohort includes 3 patients. Treatment comprises 3 primary injections (days, 1, 15 and 29), a day 64 vaccination and from there a maintenance treatment every 2 months (see Figure 4). No dose limiting toxicity, or any significant vaccination related adverse event have been reported. Minor, grade 1 injection site reaction were reported with a duration of 1 day.

Overall, the treatment is well tolerated, and the study will therefore move into the expansion cohort enrolling 10 patients into the optimal biological dose, to confirm safety response and the development of PD1-antibody in correlation to response.

In planning is the combination with SOC therapy in the same patient population. This may include monoclonal AB such as a PD-L1 inhibitor or other immunotherapy agents. Patients may have either progressed on their previous therapy or lack of response to their SOC and are at high risk of progression .

Other tumor indication eligible for the treatment with immunotherapy are currently under evaluation.

REFERENCES

- **Honey, K. (2017).** "FDA Approves Fourth Immune Checkpoint Inhibitor for Bladder Cancer." Cancer Research Catalyst. The Offical Blof of the American Association for Cancer Research.
- **Sharma, P., S. Hu-Lieskovan, J. A. Wargo and A. Ribas (2017)**. "Primary, Adaptive, and Acquired Resistance to Cancer Immunotherapy." Cell **168**(4): 707-723.
- **Pravin T. P. Kaumaya, Linlin Guo, Jay Overholser, Manuel L. Penichet & Tanios Bekaii-Saab (2020)** Immunogenicity and antitumor efficacy of a novel human PD-1 B-cell vaccine (PD1-Vaxx) and combination immunotherapy with dual trastuzumab/pertuzumab-like HER-2 B-cell epitope vaccines (B-Vaxx) in a syngeneic mouse model, OncoImmunology, 9:1, DOI: 10.1080/2162402X.2020.1818437

Sponsor and Contact

Imugene Ltd, Australia, Contact via: info@imugene.com