IMPRINTER: An Open Label, Multi-Center, Dose Escalation/Expansion, Phase 1/1b Study of IMU-201 (PD1-Vaxx), a B Cell Immunotherapy as Monotherapy or in Combination With Atezolizumab With or Without Chemotherapy, in Adults With Non-Small Cell Lung Cancer (NSCLC)

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IMUGENE
Developing Cancer Immunotherapies

Abstract #: P2.08-05

Introduction

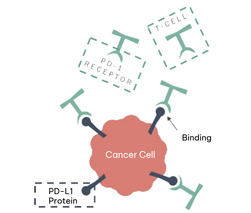
Immune checkpoint inhibitors (ICI) are part of standard of care treatment alone or in combination with chemotherapy in first-line metastatic NSCLC. However, only a subset of patients benefit from this treatment, while others develop primary or acquired resistance due to lack of T-cell response, exhaustion, or other less defined mechanisms.[1] Resistance could be overcome by combining PD-1 + PD-L1 blockade to increase tumor-specific T-cells and generate memory T-cells.[2]

- PD1-Vaxx is a B cell immunotherapy which stimulates polyclonal antibodies against PD-1 leading to active immunization and induction of memory B-cell and T-cells.
- PD1-Vaxx significantly reduced tumor growth and exhibited no toxicity or autoimmunity in preclinical models.[3,4]
- Atezolizumab is a monoclonal antibody that targets PD-L1 and is approved for the treatment of NSCLC.
- The IMPRINTER study seeks to evaluate the safety, tolerability, and initial clinical benefit of adding PD1-Vaxx to atezolizumab with and without chemotherapy in advanced or metastatic NSCLC.

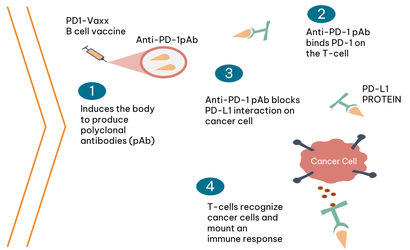
PD1-Vaxx Mechanism of Action

PD-L1 binding to PD-1 prevents T-cell recognition and killing of cancer cells

PD1-Vaxx stops cancer cells from staying undetected by T-cells



Cancer cells express PD-L1 which binds to the PD-1 receptor on T-cells



Key Eligibility Criteria

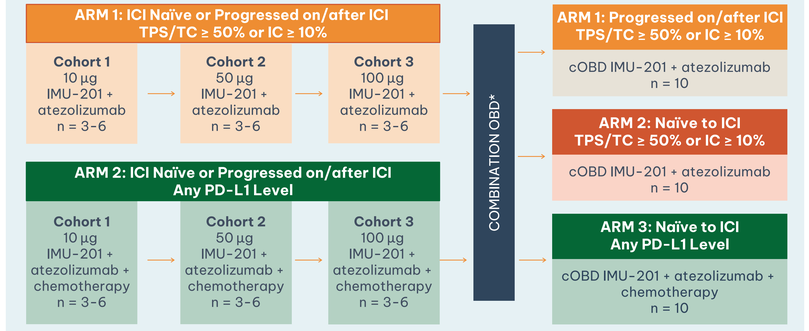
Inclusion Criteria	Exclusion Criteria
✓ Adults ≥ 18 years with histologically confirmed stage IIIB/IV NSCLC	× NSCLC expressing epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), B-Raf proto-oncogene (BRAF) or ROS proto-oncogene 1 (ROS1) mutations who have NOT received appropriate therapies targeting these mutations and progressed
✓ Life expectancy of at least 3 months	× Chronic immunosuppressive therapy (systemic steroids >10mg or others) within 2 weeks prior the first dose of study drug
✓ Measurable disease as per RECIST 1.1 criteria	× Any previous Grade ≥ 3 toxicity to a PD-1 or PD-L1 inhibitor
✓ Known PD-L1 expression level (testing by 22C3, SP142, or SP263)	× History of pneumonitis/interstitial lung disease requiring immunosuppressive agents or current pneumonitis/interstitial lung disease
✓ Eastern Cooperative Oncology Group (ECOG) performance status 0-1	× Known or suspected brain metastases
✓ Adequate hematologic, hepatic, and renal function	× Active, known, or suspected autoimmune disease

IMPRINTER Study Design

TRIAL	PATIENTS	STUDY ARMS
➢ Phase 1/1b ➢ Open Label ➢ 2 countries (US/AU) ➢ Treat until progression or toxicity	➢ Stage IIIB/IV NSCLC ➢ Phase 1: 2L+; progressed on or after immune checkpoint inhibitor (ICI) therapy ➢ Phase 1b: progressed after ICI therapy or treatment naïve	➢ Phase 1: Monotherapy ➢ Phase 1b: PD-Vaxx + atezolizumab OR PD-Vaxx + atezolizumab + chemotherapy

Phase 1: PD1-Vaxx Monotherapy Dose Escalation & Expansion
2L+ NSCLC Progressed on/after ICI, TPS/TC ≥ 50% or IC ≥ 10%

Phase 1b: PD1-Vaxx NSCLC Combination Dose Escalation & Expansion



mOBD = monotherapy optimal biological dose.
cOBD = combination optimal biological dose.
**cOBD will be determined per arm.*

Phase 1 Monotherapy Dosing

PD1-Vaxx Monotherapy

Visit Number	Visit 1 (Screening)	2	3	4	5	6	7	8	9
Study Day	-21 to -1	1	8	15	22	29	36	43	64
PD1-Vaxx administration									*

*PD1-Vaxx administered on Days 1, 15, 29, 64, every 63 days from Visit 9 onwards. Treat to progression.

Phase 1b Combination Dosing

PD1-Vaxx + Atezolizumab +/-Chemotherapy

21-Day Cycle	PD1-Vaxx Induction		Cycle 1			Cycle 2			Cycle 3+		
Cycle Day	1	8	1	8	15	1	8	15	1	8	15
Study Day	1	8	15	22	29	36	43	50	57	64	71
PD1-Vaxx administration									*		
Atezolizumab			✓		✓		✓		✓		✓
(± Chemotherapy)			SOC								

*PD1-Vaxx administered on Days 1, 15, 29, 57, and then Day 1 of every 3rd cycle (C6D1, C9D1, etc.) until disease progression or end of treatment.
Atezolizumab administered every 2 weeks; standard of care (SOC) chemotherapy.

PD1-Vaxx + Atezolizumab + Chemotherapy

28-Day Cycle	PD1-Vaxx Induction		Cycle 1				Cycle 2				Cycle 3+			
Cycle Day	1	8	1	8	15	22	1	8	15	22	1	8	15	22
Study Day	1	8	15	22	29	36	43	50	57	64	71	78		
PD1-Vaxx administration									*					
Atezolizumab			✓		✓		✓		✓		✓		✓	
Chemotherapy			SOC											

*PD1-Vaxx administered on Days 1, 15, 29, 57, and then Day 1 of every other cycle (C4D1, C6D1, etc.) until disease progression or end of treatment.
Atezolizumab administered every 2 weeks; standard of care (SOC) chemotherapy.

Study Objectives

Phase 1 PD1-Vaxx Monotherapy	Monotherapy Dose Escalation	Monotherapy Dose Expansion
Phase 1b PD1-Vaxx Combination Therapy	**Combination Dose Escalation**	**Combination Dose Expansion**
Primary Objective(s)	• Safety/Tolerability • Identify optimal biological dose (OBD)	• Anti-tumor efficacy
Secondary Objective(s)	• Antitumor efficacy	• Antitumor efficacy (additional parameters) • Safety/Tolerability
Exploratory Objective	• Immunological changes	• Immunological changes

References

1. Yost, K.E., et al. Clonal replacement of tumor-specific T-cells following PD-1 blockade. Nature medicine. 2019;25(8):1251-1259. **2.** Burrack, A.L., et al. Combination PD-1 and PD-L1 blockade promotes durable neoantigen-specific T-cell-mediated immunity in pancreatic ductal adenocarcinoma. Cell reports. 2019;28(8):2140-2155. **3.** Bekaii-Saab, T., et al. Abstract 1453: Development of a novel PD-1 vaccine and in combination with two Chimeric HER-2 peptide vaccine provides synergistic inhibition of tumor growth in a syngeneic Balb/c model challenged with CT26/HER-2 carcinoma cell line." Cancer Research 79(13 Supplement): 2019;1453-1453. **4.** Kaumaya, P. T. P., et al. Antitumor activity, immunogenicity and safety of a novel PD-1 vaccine in combination with two chimeric HER-2 peptide vaccine in syngeneic Balb/c, C57Bl/6 models and in beagle dogs. Annals of Oncology. 2019;30: v497-v498.

Study Information

ClinicalTrials.gov Number: NCT04432207

Status: Enrolling

Sites: United States, Australia