Preliminary clinical results of a therapeutic cancer vaccine PDC*lung01 in combination with anti-PD-1 in patients with Stage IV NSCLC

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On behalf of all the study investigators:

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Disclosures

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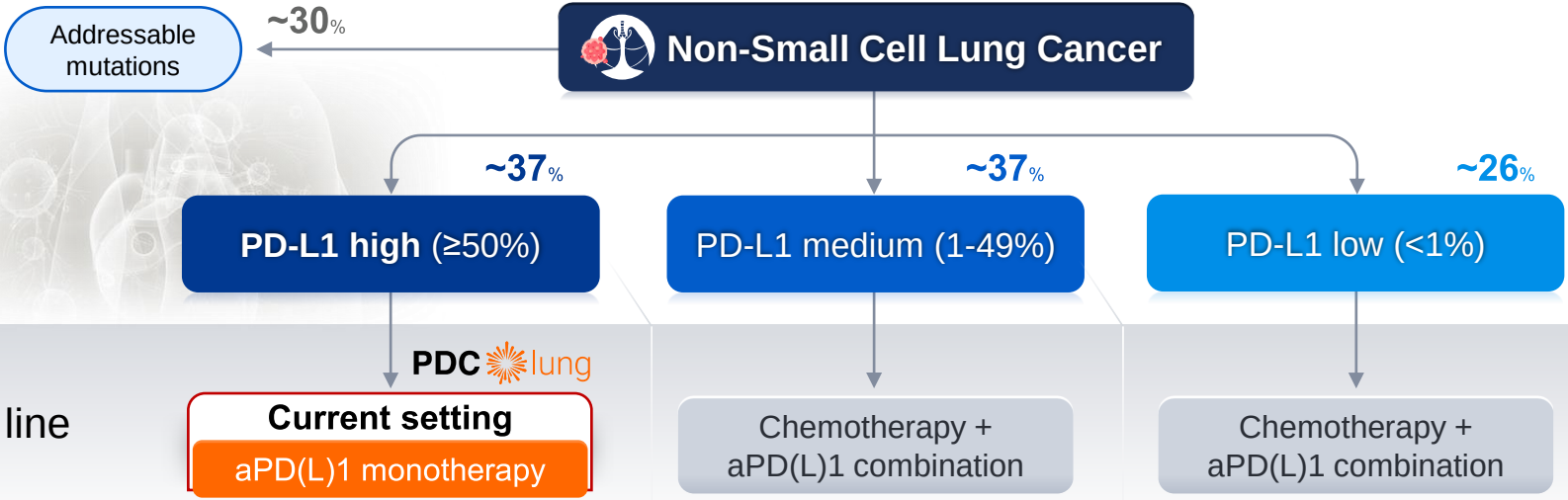
PDC*lung01 as a cancer vaccine for advanced stage NSCLC

Clinical positioning of PDC*lung was based on unmet medical need and combination strategy



Current SoC for Stage IV NSCLC
w/o addressable mutations

- ☑ **PD-L1 ≥50%: aPD(L)1**
- ☑ **PD-L1 <50%: aPD(L)1 + chemo**

PDC*line platform

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PCB
Primary cell bank

MCB
Master cell bank

WCB
Working cell bank

PDC line

Human PDC leukemia origin HLA-A2+ cell line

Growth in bioreactor in synthetic medium

Pulsed with tumor peptides

Irradiation
(Proliferation stopped, functionality conserved)

7 peptides loaded
NY-ESO-I, MAGE-A3, MAGE-A4, MUC-1, Survivin (BIRC5), Multi-MAGE*, Melan-A

Off-the-Shelf product
Ready-to-use
(Stored in liquid nitrogen)

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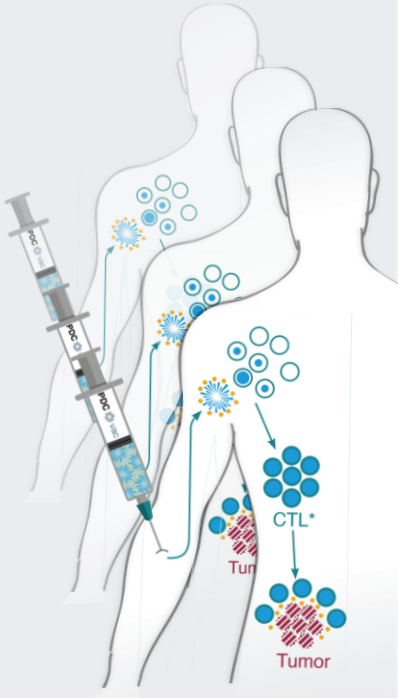
SCIENCE MEDICINES HEALTH



*Multi-MAGE: common to MAGE-A1, -A2, -A3, -A4, -A6, -A10, and -A12

Plumas et al, 2022

PDC-LUNG-101, Phase II part: Evaluation of Safety, Immunological activity, and Clinical response of PDC*lung01 in combination with pembrolizumab

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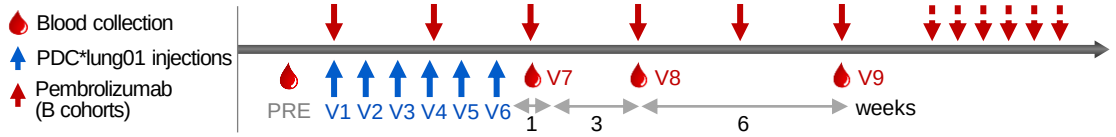
	Cohort		Arm	# of patients planned	NSCLC Patient Criteria	Main Objectives
Phase II	Pembrolizumab + PDC*lung01	**B2** High dose	20M cells/peptide **+ pembrolizumab**	42	• **Stage IV** starting **anti-PD-1** as **first-line (TPS≥50%)** • **HLA-A*02:01 positive**	• **Dose range** • **Clinical activity:** - **Overall Response Rate (ORR)** - **Median Progression Free Survival (mPFS)** - **Disease Control Rate (DCR)**

PDC*lung01 administration:
Injection regimen
: IV+SC every week x 6 times

Pembrolizumab administration:
IV, every 3 weeks (until progression)

Treatment and blood sample schedule



Interim analysis on 19 patients evaluable for 9mPFS (step1) from Cohort B2

- Protocol pre-specified Sargent 2-stage design with primary analysis population being **9 months PFS** in cohort B2 (type I error at one-sided of 0.1 and type II error level at 0.3 (power of 70%)

- Interim analysis to be performed when the 19th evaluable patients reached the 9mPFS (referred as cohort B2 [step 1])
  - Futility threshold is set to 7/19 or 37% are progression-free at 9 months
  - ORR is also considered with same type I and II error and futility threshold is set to 6/19 or 32%

- Out of 21 patients (Intent to treat population, ITT) analyzed, **19 patients** were evaluable (per protocol population)

- Database lock on **3 July 2023**

Cohort B2: Patient characteristics

Demographics and baseline characteristics		Dosed in B2 cohort N = 38
Gender	Male	23 (61%)
	Female	15 (39%)
Age	Median	69
	Range	51-82
Smoking status	Current	8 (21%)
	Past	28 (74%)
	Non-smoker	1 (2,5%)
	Missing	1 (2,5%)
ECOG PS	0	11 (29%)
	1	27 (71%)
PD-L1 expression	Median	70
	Range	50-100

Disease and treatment history		Dosed in B2 cohort N = 38
Time since initial diagnosis (mths)	Median	1.4
	Range	0.4 – 83
Tumor stage at current diagnosis	IVA	16 (42%)
	IVB	22 (58%)
Histopathology subtype	SCC	8 (21%)
	Adenocarcinoma	28 (74%)
	Other	2 (5%)
Brain metastases	Yes	6 (16%)
	No	32 (84%)

Cohort B2: Summary of safety information

Overview adverse events / SAE's and DLT	Dosed in B2 cohort N = 38					
	Total N (%)	Grade1 N (%)	Grade2 N (%)	Grade3 N (%)	Grade4 N (%)	Grade5 N (%)
Dose limiting toxicity (DLT)	1 (3%)	G4 anaphylactic reaction (post dose2)				
Pts with at least 1 TEAE	36 (95%)	10 (26%)	16 (42%)	6 (16%)	2 (5%)	2 (5%)
Pts with at least 1 related TEAE	28 (74%)	16 (42%)	11 (29%)	0	1 (3%)	0
Pts with at least ≥ G3 related AE	2 (5%)	G4 anaphylactic reaction G3 cholangitis (non-TEAE)				
Pts with at least one fatal AE	3 (8%)	G5 dyspnoea (stent dislocation) – unlikely related G5 Arrythmia – not related G5 Immune mediated pneumonitis – unlikely related (non-TEAE)				
Pts with SAE reported	13 (34%)					
Pts with TEAE leading to IMP delay	7 (18%)	G2 Atrial fibrillation G3 empyema G2 COPD exacerbation G3 pneumonia G2 Influenza A pneumonia AND G3 Bacterial prostatitis G2 urinary tract infection G2 Acute Bronchitis				
Pts with TEAE leading to IMP discontinuation	2 (5%)	G4 anaphylactic reaction (post dose2) - related G3 peripheral sensory neuropathy (post dose 5) – not related				

n (%) = number (percentage) of patients in a given category

Cut-off 03July2023

Overall mild safety profile achieved (all cohorts)

Cohort		Safety profile
Monotherapy	A1 (6 pts) (low dose)	• ***No*** DLT(Dose Limiting Toxicity) • ***No*** grade 3 or above related
	A2 (12 pts) (high dose)	
Combination with pembrolizumab	B1 (7 pts) (low dose)	• ***No*** dose effect observed on the frequency of treatment related TEAE • **One** grade 3 related*
	B2 (38 pts) (high dose)	• **One** grade 3 related* • **One** grade 4 related** → Anaphylactic reaction (after dose 2)

Based on the current data (63 patients) of PDC*lung01 in monotherapy (18 patients) or in combination with pembrolizumab (45 patients), **an overall mild safety profile was confirmed**

* Immune-mediated encephalopathy (developed after 6 months), cholangitis (at V8) ** Anaphylactic reaction (after dose 2)

Cohort B2 (Step1): Promising clinical response

Objective response rate (RECIST v1.1)		Per protocol population dosed in B2 cohort N = 19	Total treated population in B2 cohort N = 21
Best overall response	**CR**	**0**	**0**
	PR	**12 (63.2%)**	**12 (57.1%)**
	SD	**7 (36.8%)**	**8 (38.1%)**
	PD	**0**	**0**
	Missing	**-**	**1 (4.8%)**
Objective Response Rate		**12 (63.2%)**	**12 (57.1%)**
	80% binominal CI	**45.9% - 78.2%**	**41.0% - 72.2%**

Number of Progression Free Survival (PFS) events	**11 (57.9%)**	**13 (61.9%)**
PFS at 9 months - KM estimate and 80% CI (%)	**52.1** [36.5; 65.6]	**47.1** [32.7; 60.3]
Median PFS and 95% CI (in Months)	**10.9** [5.6; -]	**8.87** [5.6; -]

PP population

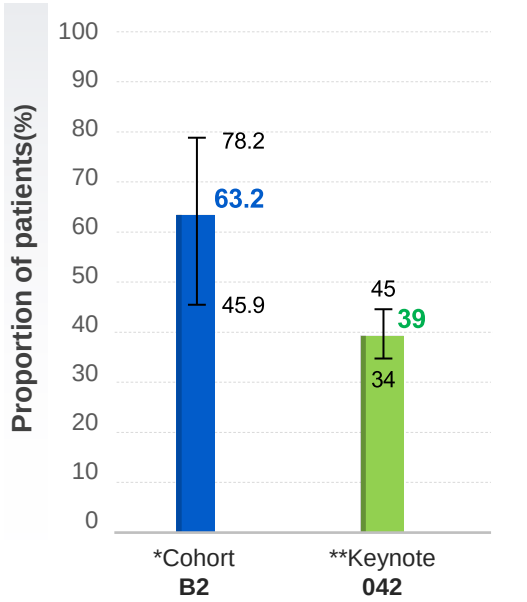
Median follow-up: **12.5 months** (95% CI: 9.9, 14.2)

Median duration of response: **9.49 months** (95% CI: 4.4, -)

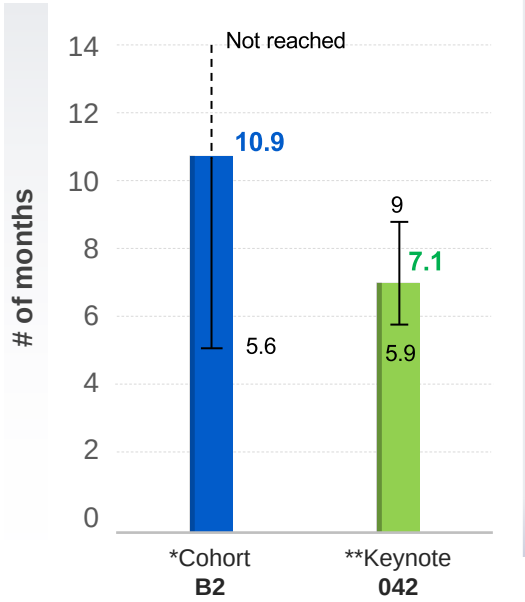
Disease control rate: **94.7%** (80% CI: 81, 99.4)

Cohort B2 (Step1): Promising clinical response

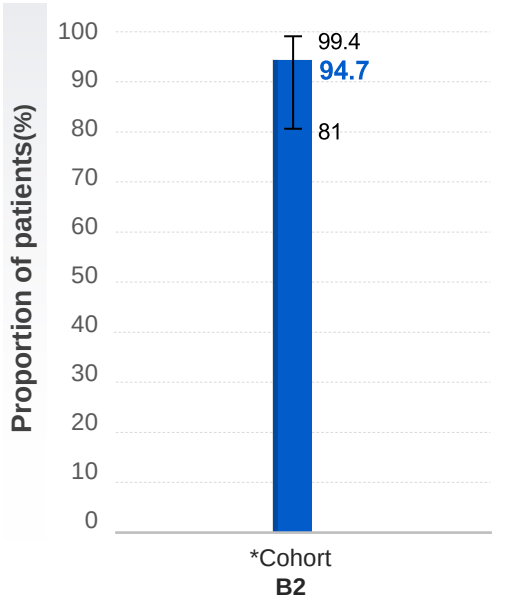
ORR
Overall Response Rate



mPFS
Median Progression Free Survival



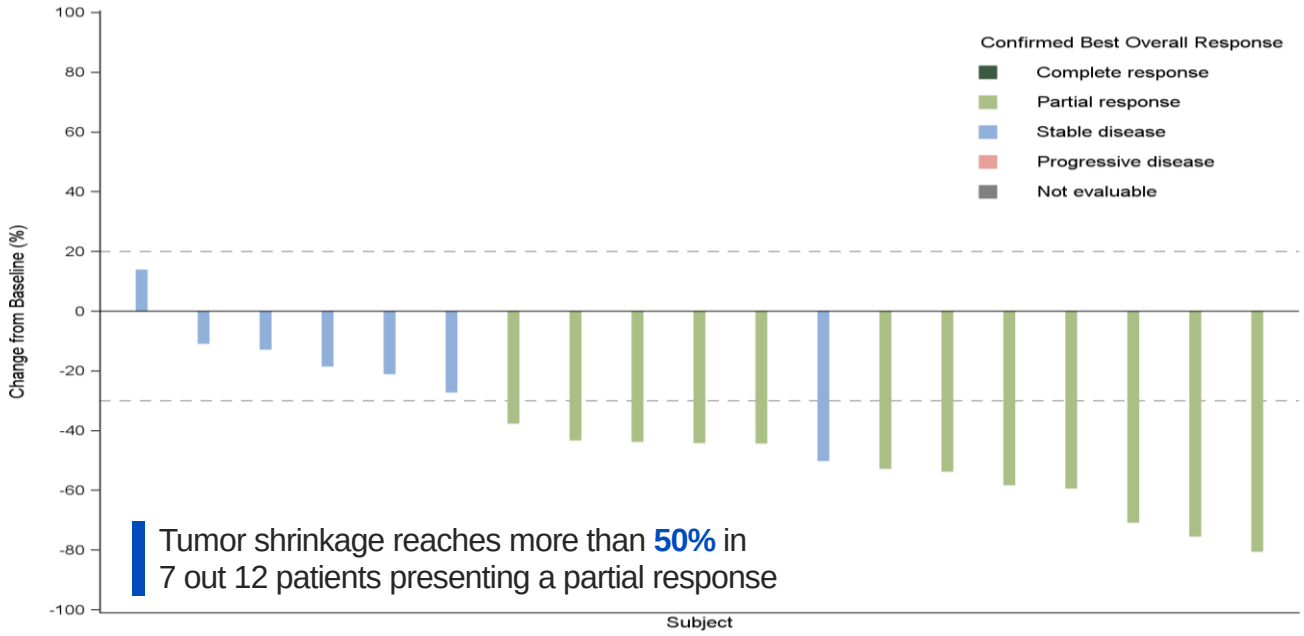
DCR
Disease Control Rate



*Cohort B2: n=19 (per procotol population); **Keynote 042, IIT population, sub-group TPS>50%, n=299

Cohort B2 (Step1): Promising clinical response

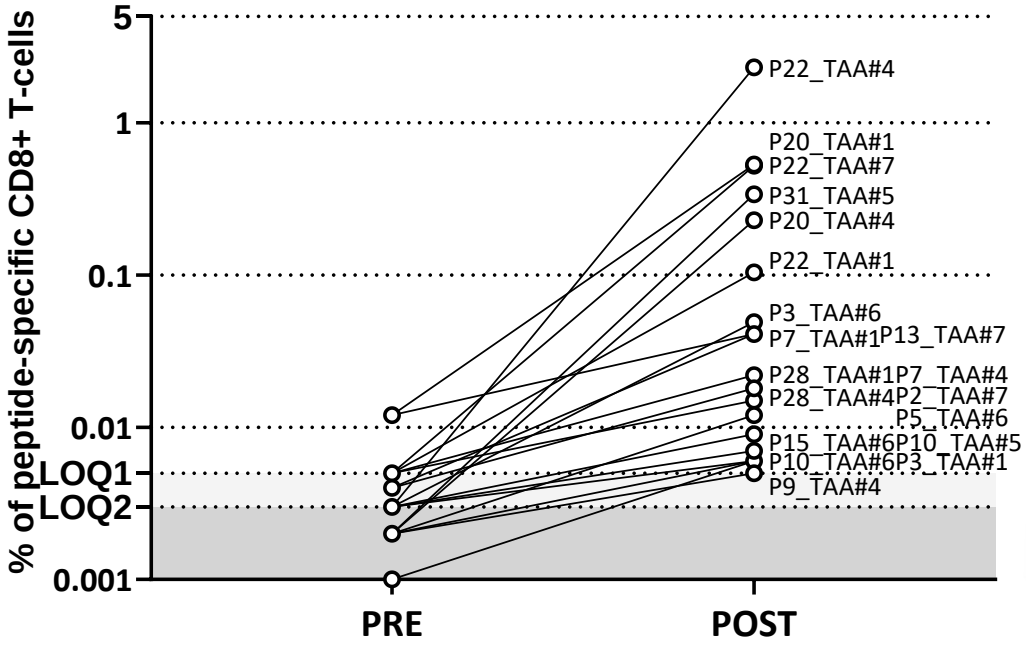
Tumor shrinkage:
*Overall Response Rate **63.2%**

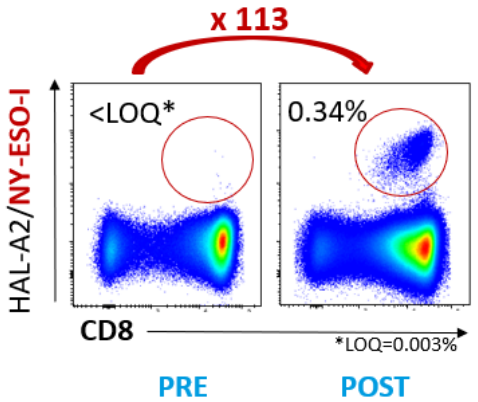


* Number of Patients – B2 interim analysis: n=19

Cohort B2 (Step1): Immunological response

- Circulating peptide-specific CD8+ T-cells are assessed without any prior in vitro stimulation





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Determination of circulating peptide-specific CD8+ T cells has been assessed on purified CD8+ T-cells using HLA-A2/peptide multimers. A limit of quantification (LOQ) was defined: 0.005% for Melan-A, Mage-A3 and Survivin, and 0.003% for other specificities

All expansions found in all positive patients are represented

PDC-LUNG-101: Immunological and clinical responses in B2 cohort

	Cohort	Partial Response	Stable Disease
Percentage of patients with expansion of antigen-specific T-cells	B2 (n=19)	6/12	6/7

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Sunday Apr 7
1:30-5:00 pm

CONCLUSION: Cohort B2 (step1)

- **Preliminary efficacy results** based on 19 evaluable patients of cohort B2 step1 (PP)

With a median follow up of 12.5 months, the ORR (63.2%), DCR (94.7%), mPFS (10.9mo) and mDOR (9.49mo) of PDC*lung01 in combination with pembrolizumab showed encouraging signals

- **Immune response analysis**

The observed immune response confirms the mechanism of action of the PDC*lung01 in relation with clinical activity

- **Safety analysis**

The safety analysis of 38 patients treated with PDC*lung01 in combination with pembrolizumab confirmed the overall mild safety profile of PDC*lung01

These interim results suggest that this combination may provide a clinical meaningful tumor response in stage IV NSCLC targeted population with a mild safety profile