2024 ESMO IMMUNO-ONCOLOGY

Annual Congress

PHASE I/II TRIAL EVALUATING THE INNOVATIVE THERAPEUTIC CANCER VACCINE PDC*LUNG01 IN COMBINATION WITH ANTI-PD-1 IN PATIENTS WITH UNTREATED STAGE IV NON-SMALL CELL LUNG CANCER

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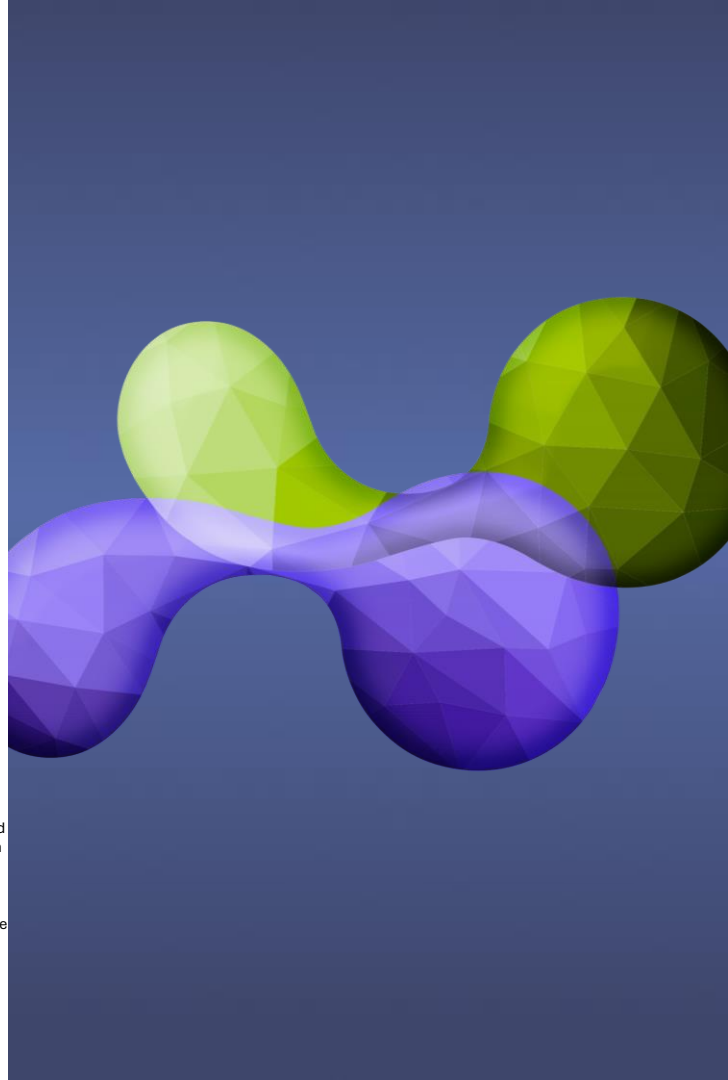
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE



Declaration of interests

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Advisory functions

- AstraZeneca, BMS, Boehringer-Ingelheim, Daiichi-Sankyo, Janssen, Merck, MSD, PDC*line Pharma, Pfizer, Roche, Sanofi, Transgene

Lectures

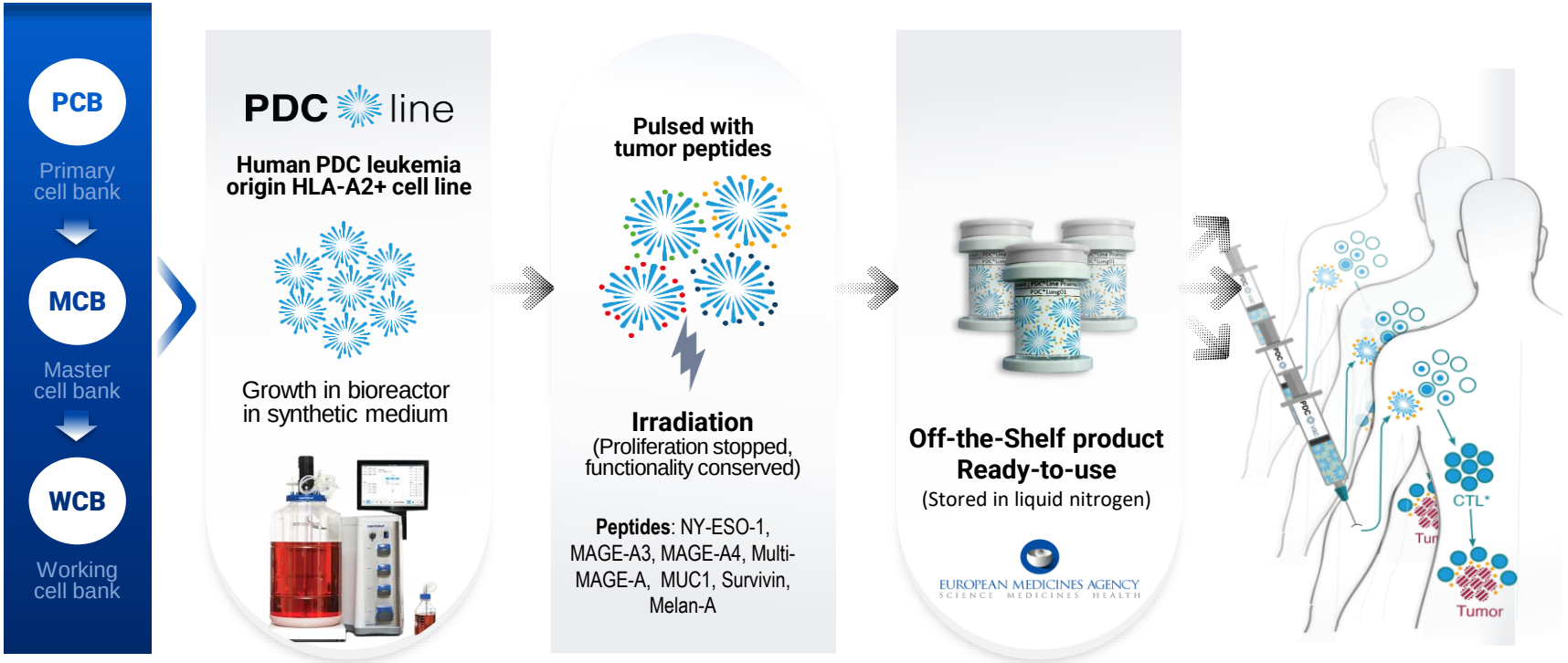
- Astra-Zeneca, BMS, Merck, MSD, Sanofi

Others

- None

PDC*line platform

Off-the-shelf allogeneic cell-based drug product with a scalable production process



Plumas et al, 2022

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PDC-LUNG-101, phase I/II trial

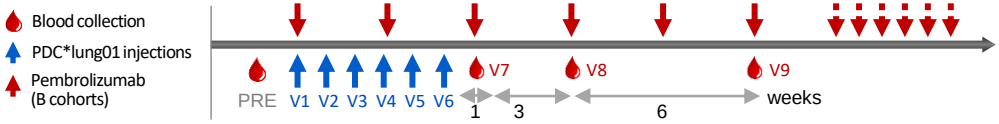
Evaluation of safety, immunological and clinical activities of PDC*lung01 +/- pembrolizumab

	Cohort		Arm	Planned patients	NSCLC patient criteria	Main endpoints
Phase I part	PDC*lung01 Mono	A1 Low dose	2M cells/peptide	6	• **Stage IIa/IIb/IIIa** after R0 resection • **Adjuvant chemotherapy**	• **Safety & tolerability** • **Immune activity**
		A2 High dose	20M cells/peptide	10		
Phase II part	Anti-PD-1 + PDC*lung01	B1 Low dose	2M cells/peptide + anti-PD-1	6	• **Stage IV** starting **anti-PD-1** as **first-line (TPS≥50%)** • **HLA-A*02:01 positive** • Measurable disease • ECOG 0-1 • Stable brain metastasis	• **Dose range and safety evaluation** • **Clinical activity:** **- Objective response rate (ORR)** **- 9 months progression-free survival (PFS)** **- Median PFS** **- Duration of Response (DoR)** **- Disease Control Rate (DCR)**
		B2 High dose	**20M cells/peptide + pembrolizumab**	**42**		

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

Anti-PD1 administration:
IV, every 3 weeks (until progression)

Treatment and blood sample schedule



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Demographic and baseline characteristics

Safety population, cohort B2 - PDC*lung01 high dose in combination with pembrolizumab

Demographics and baseline characteristics (pts dosed)	B2 Safety population N = 48
Male	27 (56%)
Age, median (range), y	69 (50- 83)
Smoking status Current Past Non-smoker	 12 (25%) 34 (71%) 2 (4%)
ECOG PS 0 1	 13 (27%) 35 (73%)
PD-L1 expression ≥50%, median (range)	70 (50-100)

Disease history (pts dosed)	B2 Safety population N = 48
Time since initial diagnosis, median (range), months	1.3 (0.5 - 83.0)
Tumor stage at current diagnosis IVA IVB	 19 (40%) 29 (60%)
Histopathology subtype Squamous cell carcinoma Adenocarcinoma NSCLC-NOS	 10 (21%) 36 (75%) 2 (4%)
Brain metastases (baseline)	
Yes	12 (25%)
No	36 (75%)

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Adverse events summary

Mild safety profile in cohort B2

Adverse Events	B2 Safety population, N=48	
	Any grade N (%)	Grades 3-5 N (%)
DLT	1 (2%)	1 (2%)
At least 1 TEAE	47 (98%)	13 (27%)
At least 1 related TEAE	40 (83%)	2 (4%)
At least ≥ G3 related AE	3 (6%)	3 (6%)
TEAE leading to IMP discontinuation	3 (6%)	3 (6%)
related	1 (2%)	1 (2%)
TEAE leading to IMP delay (all not related)	9 (19%)	3 (6%)
Immune-mediated AE grade ≥ 3	2 (4%)	2 (4%) *
AE leading to death (all not related)	3 (6%)	3 (6%)
Any SAE	14 (29%)	11 (23%)
related	3 (6%)	1 (2%)

Related TEAE > 15% of patients	B2 Safety population N = 48
Anti-HLA Ab	19 (40%)
Pyrexia	10 (21%)
Fatigue	9 (19%)

G4 anaphylactic reaction (post dose 2)
G3 immune-related cholangitis (non-TEAE)
G3 asthenia

G4 anaphylactic reaction (post dose2) - DLT

* G5 immune-mediated pneumonitis (not related, non-TEAE) - G3 immune-related cholangitis (non-TEAE)

DLT: dose limiting toxicity; TEAE: treatment emergent adverse event

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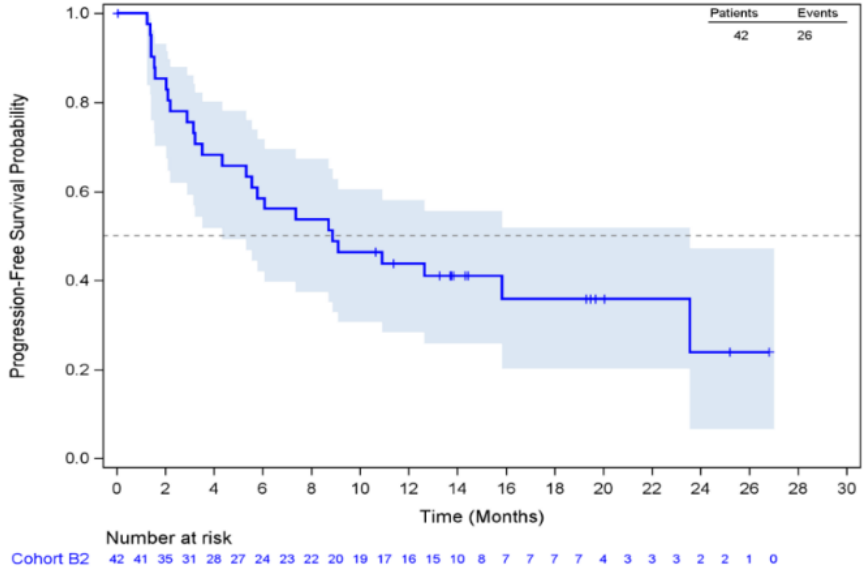
Cohort B2 clinical activity: primary analysis of ORR and PFS

Designed Per Protocol (DPP) population: 42 evaluable* patients

Median follow-up time **19.5 months** (95%CI: 13.8-25.6)



Efficacy endpoints	B2 cohort (DPP population) N=42		Keynote-042*** (PD-L1≥50%) N=299
Confirmed objective response rate, N (%)	**23 (55%)**	**Δ16%**	117 (39%)
CI	**80% CI [43.7-65.4]**		95% CI [33.6-44.9]
Median duration of response, months	**Not reached**		28.1
CI	**[7.7-not reached]**		[2.1-70]
DCR*, N (%)	**34 (76%)**		-
CBR, N (%)**	**27 (64%)**		-
PFS at 9 months (%)	**49%**		-
CI	**80% CI [38.5-58.3]**		
Median PFS, months	**8.87**	**Δ2.4m**	6.5
CI	**95% CI [4.3-23.6]**		95% CI [5.9-8.6]

* Evaluable patient is defined as patient who received at least 5 doses of vaccine, and had one post-baseline tumor assessment

*DCR: Disease control rate defined as confirmed responders + pts with stable disease for at least 3 months duration (per protocol definition)
** CBR: Clinical benefit rate defined as confirmed responders + pts with stable disease for at least 6 months duration
***De Castro, JCO 2022

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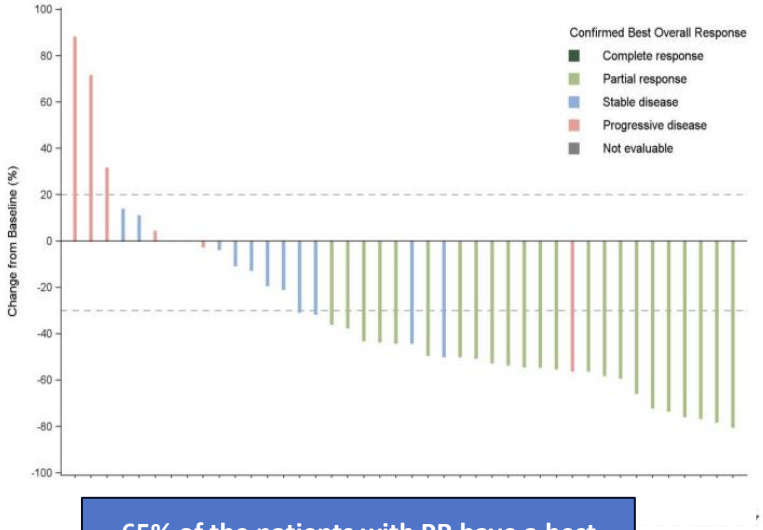
Cohort B2 clinical activity: primary analysis of ORR and PFS

Durable clinical responses in advanced stage NSCLC patients

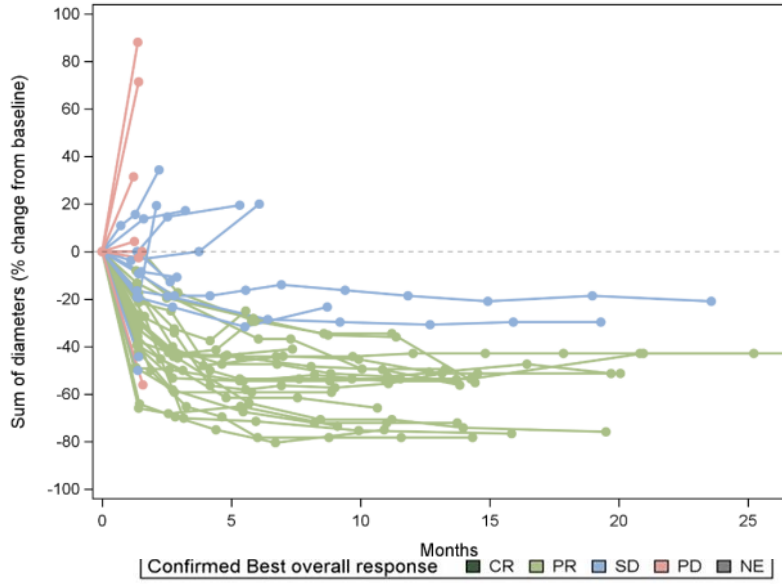
Median follow-up time **19.5 months** (95%IC: 13.8; 25.6)

Tumor shrinkage: Best change in target lesion for 42 evaluable patients



65% of the patients with PR have a best change in target lesion reduction over 50%

Spider Plot of 42 evaluable patients: ORR of 55%



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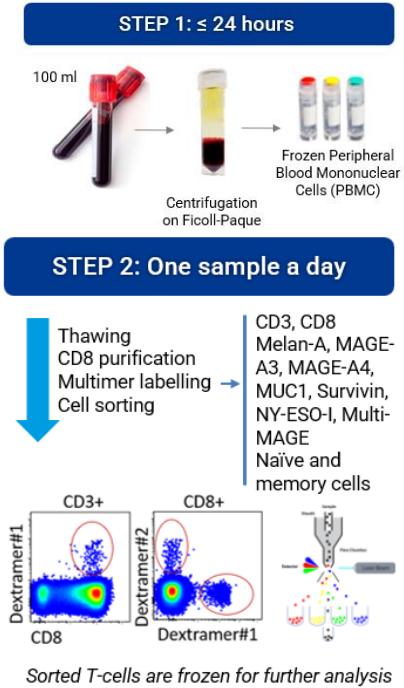
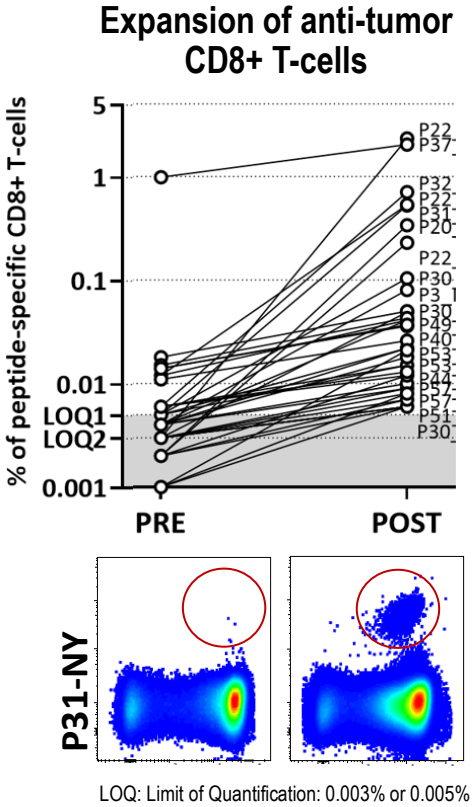
Cut-off date 18Jul24

Immune response and correlation with PFS

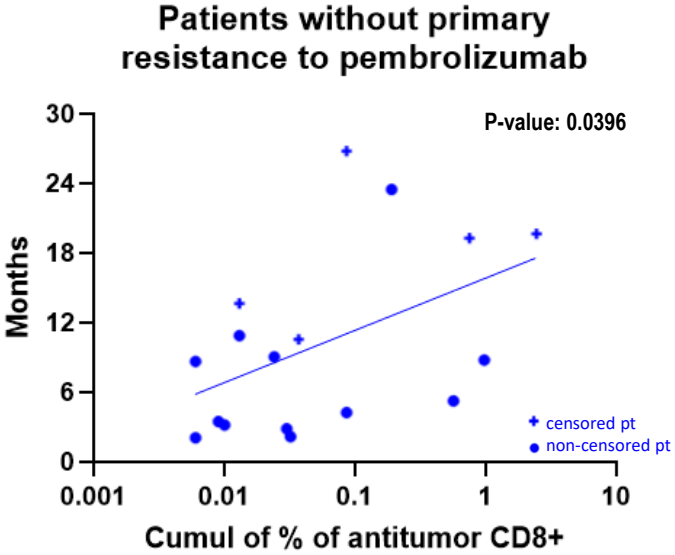
- **Circulating** peptide-specific anti-tumor CD8+ T-cells **without any prior in vitro stimulation** evaluated by flow cytometry



Sorted T-cells are frozen for further analysis



LOQ: Limit of Quantification: 0.003% or 0.005%



- **Relationship between PFS and expansion of anti-tumor CD8+ T- cells**

Spearman correlation r=0.571, nXY pairs=17

Conclusions

PDC*lung01 plus pembrolizumab may provide a meaningful clinical activity and has a mild safety profile

→ **PDC*lung01+pembrolizumab promising based on cohort B2 ORR and PFS results vs. pembrolizumab alone in KN-042**

- Pre-specified objective of 15% increase in ORR of designed per protocol population reached (55% vs pembro alone 39% in KN-042)
- 36% relative improvement for design per protocol population on mPFS (+2.4 months increase vs pembro alone in KN-042)
- Other clinical endpoints encouraging (DCR 76%, CBR 64%). Median duration of response and overall survival not mature

→ **Related TEAEs mostly grade 1-2, with one related TEAE grade 4**

– Only 2% of related TEAEs leading to discontinuation (vs 9.1% for pembrolizumab alone in KN-042)

→ **Significant immune response with indications of a relationship with clinical outcome in cohort B2**

- Positive antigen-specific CD8+ T-cell response detected in 56% of patients, with remarkable expansions up to 2.3% of total CD8+T-cells.
- Significant correlation between the amplitude of antigen-specific CD8+ T-cell response and the PFS

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