Open-label, dose-escalation, phase I/II study to assess the safety, tolerability, immunogenicity and preliminary clinical activity of the therapeutic cancer vaccine PDC*lung01 with or without anti-Programmed Death-1 (PD-1) treatment in patients with non-small-cell lung cancer (NSCLC)

1176P

J.Vansteenkiste[1], I. Demedts[2], E. Pons-Tostivint[3], B. Biesma[4], F. Borm[5], B. Colinet[6], K. Cuppens[7], S. Derijcke[8], L. Greillier[9], J. Jurgens[10], D. Moro-Sibilot[11], M. Pérol[12], M. Sebastian[13], M. Skrzypski[14], W.Theelen[15], C.Van De Kerkhove[16], M. Collodoro[17], J. Plumas[17], C. Debruyne[17], A. Sibille[18]

*1. Department of Respiratory Oncology, University Hospitals KU Leuven, Belgium; 2. Department of Pulmonary Diseases, AZ Delta Roeselare, Belgium; 3. Medical Oncology, Nantes University, Nantes, France; 4. Department of Pulmonary Diseases, Jeroen Bosch Ziekenhuis, The Netherlands; 5. Department of Pulmonology, Leiden University Medical Center, Leiden, The Netherlands; 6. Pneumology and oncology unit, Grand Hôpital de Charleroi (GHdC), Charleroi, Belgium; 7. Department of Pulmonology and Thoracic oncology, Jessa Hospital, Hasselt, Belgium; 8. Department of Thoracic Oncology/Pulmonology, AZ Groeninge Kortrijk, Belgium; 9. Aix Marseille Univ, APHM, Marseille, France; 10. Kliniken der Stadt Koeln gGmbH, Lungenklinik Koeln- Merheim, Germany; 11. Thoracic Oncology unit, SHUPP, CHU Grenoble Alpes, France; 12. Department of Medical Oncology, Léon Bérard Cancer Centre, Lyon, France; 13. Dept. of Medicine, Hematology & Oncology, University hospital Frankfurt, Germany; 14. Department of Oncology and Radiotherapy, Medical University of Gdańsk, Poland; 15. Department of Thoracic Oncology, The Netherlands Cancer Institute, Amsterdam, The Netherlands; 16. Department of Pulmonology and Thoracic oncology, Vitaz Sint-Niklaas, Belgium; 17. PDC*line Pharma SAS, France 18. Department of Pulmonology, University Hospital of Liège, Liège, Belgium*

Background and rationale

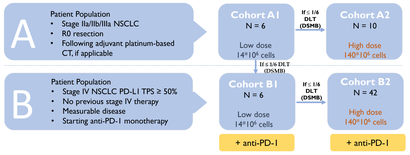
- Anti-PD-(L)1 antibodies are the cornerstone of treatment for advanced NSCLC. However, a substantial number of patients do not benefit from PD-(L)1 blockade when used in monotherapy
- Boosting antitumor cytotoxic CD8+ T cells represents a promising approach to potentiate their efficacy
- PDC*lung01 is a therapeutic cancer vaccine consisting of an irradiated plasmacytoid dendritic cell line (PDC*line), loaded with HLA-A*02:01 restricted peptides (PDC*vac)
- The 6 selected peptides are encoded by antigens expressed in NSCLC: NY-ESO-1, MAGE-A3, MAGE-A4, Multi-MAGE-A, MUC1, Survivin. Melan-A is used as a positive control of PDC*lung01-induced immunogenicity
- PDC*line is a professional antigen presenting cell able to prime and expand peptide-specific CD8+ T cells in vitro and in vivo, and is synergistic with anti-PD-1 antibodies [Lenogue 2021; Plumas, 2022]

Methods

- Open-label, multicentre, dose-escalation, phase I/II study with PDC*lung01 administered weekly by subcutaneous and intravenous route for 6 consecutive doses
- Two dose levels: $14*10^6$ cells (Low Dose) and $140*10^6$ cells (High Dose), split equally in two administration routes
- NSCLC patients positive for HLA-A02:01 at pre-screening are enrolled in 4 cohorts
  Resected stage II/IIIA in adjuvant setting treated with low dose (A1) or high dose (A2) of IMP as single agent following standard of care;
  Stage IV NSCLC with measurable disease, PD-L1 tumour proportion score ≥50% and no targetable driver mutation, treated with low dose (B1) or high dose (B2) of IMP in combination to pembrolizumab.
- Study endpoints: safety, tolerability and immune response in all patients; clinical activity for B cohorts.

We report here on the first 3 cohorts (A1/A2/B1) that have been completed

Study flow chart



Dose limiting toxicities: definition

- All CTCAE Grade 4 and 5 toxicities
- CTCAE Grade 3 toxicities
  Non-haematological toxicity (not laboratory) lasting > 48 hours despite optimal treatment
  Non-haematological laboratory value in case of
  Medical intervention required
  Hospitalization
  Clinically relevant and persisting > 48 hours
  Cytokine Release Syndrome persisting > 48 hours despite treatment
  Allergic reaction and/or anaphylaxis and/or infusion related reaction occurring within 24 hours post-injection

Results

- At data cut-off (16 May 2022), cohorts A1/A2/B1 were completed, cohort B2 is ongoing
- 25 patients (6 in A1, 12 in A2 and 7 in B1) started treatment, 22 received at least 5 doses and were evaluable

Demographics

Demographics and baseline characteristics		Dosed in A1/A2 cohort N = 18	Dosed in B1 cohort N = 7
Gender	Male	15 (83%)	4 (57%)
	Female	3 (17%)	3 (43%)
Age	Median	64	64
	Range	40-71	39-78
Smoking status	Current	1 (6%)	1 (14%)
	Past	17 (94%)	5 (71%)
	Non-smoker	-	1 (14%)
ECOG PS	0	10 (56%)	3 (43%)
	1	8 (44%)	4 (57%)
PD-L1 expression	Median		80
	Range		50-100

Disease and treatment history		Dosed in A1/A2 cohort N = 18	Dosed in B1 cohort N = 7
Tumor stage at current diagnosis	IIA	2 (11%)	
	IIB	9 (50%)	
	IIIA	7 (39%)	
	IVA		3 (43%)
	IVB		4 (57%)
Histopathology subtype	Squamous carcinoma*	6 (33%)	2 (28%)
	Adeno carcinoma	12 (67%)	3 (43%)
	Other		2 (28%)
Adjuvant Chemo	Yes	16 (89%)	
	No	2 (11%)	
Brain metastases	Yes		2 (29%)
	No		5 (71%)

*All demographics and baseline characteristics were similar in A1 and A2, except for the rate of squamous cell carcinoma.

Safety overview

Overview adverse events / SAE's and DLT	Number of patients (%) Dosed in A1/A2 cohort (N=18)			Number of patients (%) Dosed in B1 cohort (N=7)			
	Total	Grade1	Grade2	Total	Grade1	Grade2	Grade3
Dose limiting toxicity (DLT)	-			-			
Pts with at least 1 related TEAE*	**16 (89%)**	10 (56%)	6 (33%)	**6 (86%)**	5 (71%)	1 (14%)	-
Pts with at least 1 related SAE**	-	-	-	**1 (16%)**	-	-	1 (16%)
Pts with at least 1 non-related SAE	**2 (11%)**			**4 (57%)**			
Pts with AE leading to IMP interruption	**1 (6%)**	Injection pain		-			
Pts with AE leading to IMP delay	**1 (6%)**	Rhinitis/cough		-			
Pts with AE leading to IMP discontinuation	-			**1**	Progression of disease		

* TEAE: treatment emergent adverse events (adverse events occurring from first IMP dose till 28 days post last IMP dose)
** Treatment related SAE Grade 3 : immune-mediated encephalopathy starting 6 months after end of treatment in the B1 cohort (pembrolizumab + IMP)

Related treatment-emergent AEs >10% of patients

Treatment Emergent Adverse events by MedDRA System Organ Class (SOC)	Dosed in A1/A2* cohort N = 18	Dosed in B1 cohort N = 7
Anti-HLA antibody test against PDC*lung01	11 (61%)	-
Injection site reactions	8 (44%)	1 (14%)
Fatigue	2 (11%)	3 (43%)
Dysgeusia	1 (6%)	3 (43%)
Pyrexia	2 (11%)	1 (14%)
Malaise	1 (6%)	1 (14%)
Chills	1 (6%)	1 (14%)
Neutropenia	2 (11%)	-
Pruritis	2 (11%)	-
Musculoskeletal stiffness	-	1 (14%)

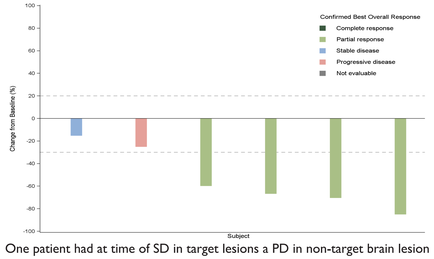
*Treatment emergent adverse events were similar in A1 (low dose) and A2 (high dose), except for anti-HLA antibodies that were mainly observed in the high dose cohort

Tumor response and PFS per investigator for B1 cohort

Objective response rate (RECIST v1.1)		Per protocol population dosed in B1 cohort N = 6
Best overall response	CR	0
	PR	4 (66.7%)
	SD	1 (16.7%)
	PD	1 (16.7%)
	NE	
Objective Response Rate		4 (66.7%)
	80% binominal CI	33.3% - 90.7%

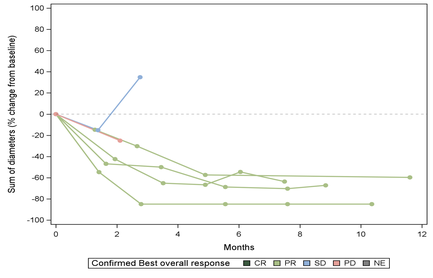
Number of Progression Free Survival (PFS) events	2 (33.3%)
PFS at 9 months - KM estimate and 80% CI (%)	66.7 [36.4; 85.0]

Best change from baseline per investigator for B1 cohort

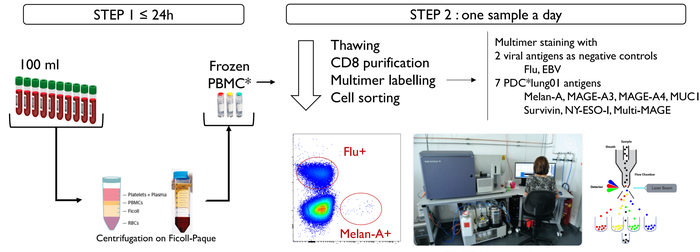


One patient had at time of SD in target lesions a PD in non-target brain lesion

Change in target lesions over time

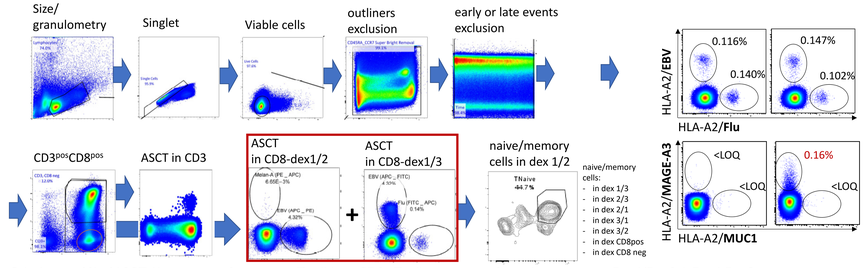


Overview of the immuno-monitoring workflow



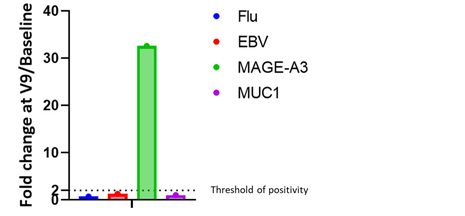
*Peripheral Blood Mononuclear Cells

Gating strategy of the antigen specific T-cells (ASCT)

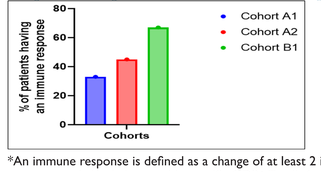


Calculation of % of ASCT (Antigen-specific cytotoxic T cells) on CD8+ T-cells as a mean of two determinations Dex1/Dex2 & Dex1:Dex3

Cohort B1 case report: expansion of MAGE-A3 specific T-cells



Proportion of patients with an immune response*



*An immune response is defined as a change of at least 2 in the percentage of circulating peptide-specific CD8+ T cells for any of the PDC*lung01 peptides between baseline and V7, V8 or V9

Conclusions

Treatment with the therapeutic cancer vaccine PDC*lung01

- Is feasible with an acceptable safety profile
- Is found to be biologically active to trigger an antitumor immune response in a significant number of patients
- Is associated with a promising objective response rate in combination with pembrolizumab in first line setting in stage IV patients, with the caveat of low numbers at the present time

Study information/disclosures

Protocol Number: PDC-LUNG-101 | Status: Recruiting | Clinical Trial Identification: NCT03970746 | Acknowledgements: This study is sponsored by PDC*line Pharma SAS. | Disclosure Statement: Prof. Dr. J. Vansteenkiste declares advisory board functions for PDC*line Pharma |

Contact info: c.debruyne@pdc-line-pharma.com