#156

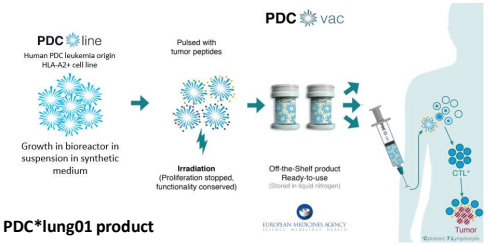
Induction of circulating antitumor specific CD8+ T cells in patients with non-small cell lung cancer treated with an allogeneic plasmacytoid dendritic-cell based cancer vaccine with or without anti- PD-1 treatment

S. Michel[1], I. Demedts[2], A. Sibille[3], E. Pons-Tostivint[4], C. Van de Kerkhove[5], S. Derijcke[6], M. Collodoro[1], K. Al Badawy[1], C. Duchayne[1], C. Debruyne[1], M. Perol[7], E.-L. Buchmeier[8], K. Cuppens[9], J. Vansteenkiste[10], J. Plumas[11]

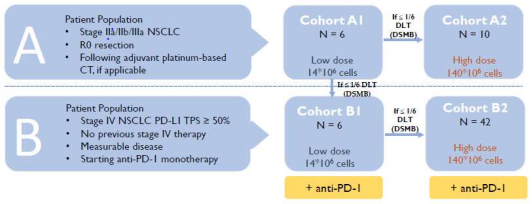
1. PDC*line Pharma, R&D, Liege, Belgium, 2. AZ Delta, Department of Pulmonary Diseases, Roeselare, Belgium, 3. University Hospital of Liège, Department of Pulmonology, Liege, Belgium, 4. Nantes University, Medical Oncology, Nantes, France, 5. Vitaz Sint-Niklaas, Department of Pulmonology and Thoracic oncology, Sint-Niklaas, Belgium, 6. AZ Groeninge, Department of Thoracic Oncology/Pulmonology, Kortrijk, Belgium, 7. Léon Bérard Cancer Centre, Department of Medical Oncology, Lyon, France, 8. Lungenklinik, Kliniken der Stadt Koeln gGmbH, Koeln- Merheim, Germany, 9. Jessa Hospital, Department of Pulmonology and Thoracic oncology, Hasselt, Belgium, 10. University Hospitals KU Leuven, Department of Respiratory Oncology, Leuven, Belgium, 11. PDC*line Pharma, R&D, La Tronche, France

PDC*lung01 Off-the-shelf plasmacytoid dendritic cell-based product

- PDC*lung01 (IMP) is a therapeutic cancer vaccine based on an irradiated plasmacytoid dendritic cell line loaded with HLA-A*02:01 restricted peptides (NY-ESO-1, MAGE-A3, MAGE-A4, Multi-MAGE-A, MUC1, Survivin and Melan-A) able to prime and expand peptide-specific CD8+ T cells *in vitro* and *in vivo*, and is synergistic with anti-Programmed Death (PD)-1 (Charles, 2020; Lenogue 2021)

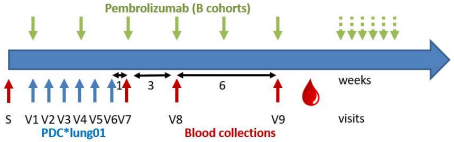


PDC-LUNG-101 study design

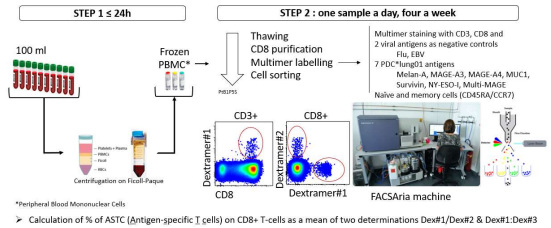


Immunomonitoring assays

- Several circulating immune parameters were monitored at different times before and after vaccination using different assays developed by PDC*line Pharma: leukocyte count and determination of peptide-specific CD8+ T cells, for which a limit of quantification (LOQ) was defined to better assess the fold changes of the cell expansion.

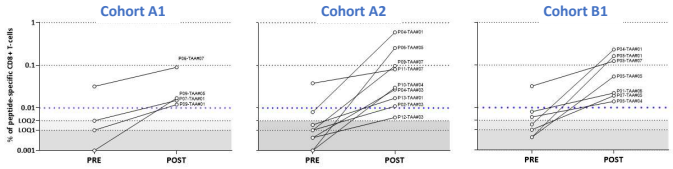


Overview of the immunomonitoring workflow

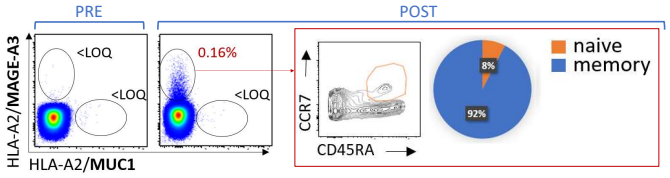


- Calculation of % of ASTC (Antigen-specific T cells) on CD8+ T-cells as a mean of two determinations Dex#1/Dex#2 & Dex#1:Dex#3

Expansion of circulating antitumor-specific CD8+ T-cells following PDC*lung01 treatment

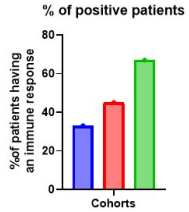


- Frequencies of circulating antigen-specific CD8+ T-cells, pre and post treatment with PDC*lung01. The proportions of tumor antigen-specific T cells targeted were generally under the Limit of Quantification (LOQ, grey zone) at baseline and over 0.01% post-vaccination.



- Expanded antigen-specific CD8+ T-cells displayed a memory phenotype

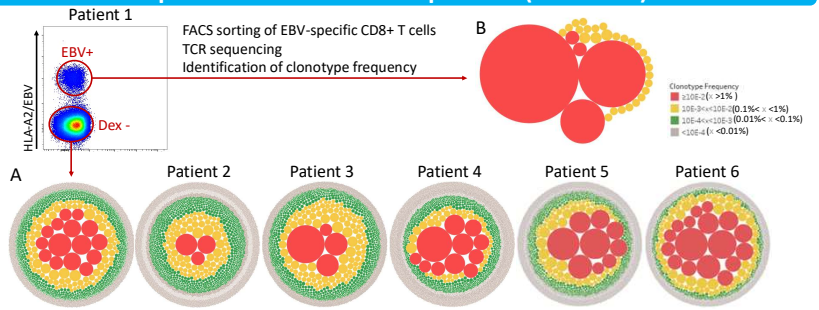
Correlation between Best Overall Response and immunological response in B1 patients



Best Overall Response		Partial Response	Stable Disease	Progressive Disease
Immunological Response	Specific CD8+ T cells for at least 1/6 lung antigen	3	1	0
	No Immune response detected	1	0	1

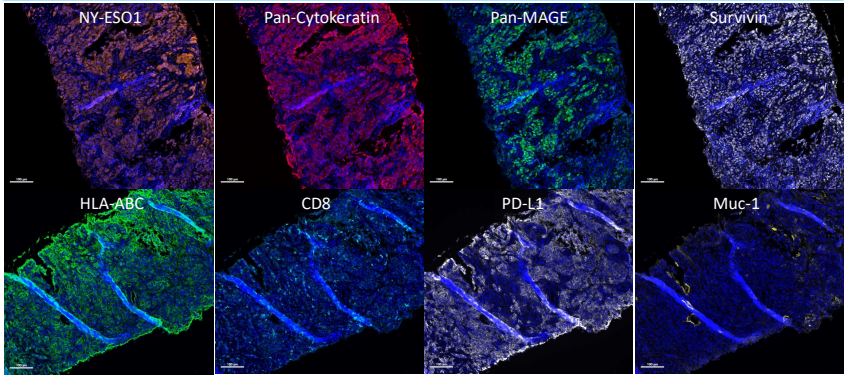
- A positive patient is defined when a change of at least 2 in the percentage of circulating peptide-specific CD8+ T cells for any of the PDC*lung01 peptides between baseline and V7, V8 or V9.

Exploration of basal TCR repertoire (cohort B1)



- Exploration of TCR repertoire and clonotype frequency in patient samples. cDNA libraries were generated using primers specific for the TCRβ CDR3 region before sequencing. Addition of a unique molecular identifier (UMI) is added to identify and quantify clonotype frequency. (A) Comparison of the global TCR repertoire between patients of cohort B1, highlighting heterogeneity in clonotype frequency. (B) Bubble chart representation of EBV-specific clonotype frequency from patient 1. As a proof of concept, HLA-A2/EBV dextramers have been used to sort EBV-specific CD8 T cells to identify and quantify associated clonotypes. Data were generated by Seqalis (Belgium)

Tumor microenvironment evaluation by multiplex IHC



- Tumor-associated antigen expression and characterization of tumor microenvironment of patients' tumor samples collected before treatment. Opal multiplex immunochemistry was performed to evaluate the expression of CD8, HLA-ABC, Pan-Cytokeratin, PD-L1 as well as tumor antigens Muc1, Survivin, Pan-Mage and NY-ESO1 (data generated by Centre Léon Bérard – France):

Pan-CK	Muc1	Surv.	Pan-Mage	NY-ESO1	PD-L1	CD8	HLA-ABC
80%	0%	100%	80%	100%	100%	30%	90%

>>> Conclusion <<<<

- PDC*lung01 is biologically active to induce an antitumor immune response in a significant number of patients, synergistic with pembrolizumab and associated with clinical responses.

Protocol Nb: PDC-LUNG-101, Status: Recruiting, Clinical Trial Identification: NCT03970746; This study is sponsored by PDC*line Pharma