Humoral response in lung cancer patients treated with a plasmacytoid dendritic allogeneic cell line-based cancer vaccine in combination with or without anti-PD1

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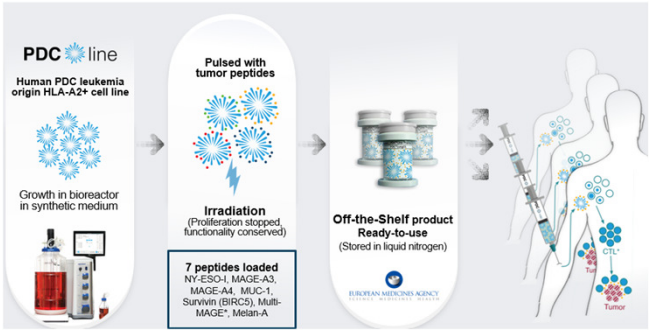
PDC*lung01
Off-the-shelf plasmacytoid dendritic cell-based product

- PDC*lung01 (IMP) is a therapeutic cancer allogeneic 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* (Plumas, Current Opinion in Oncol, 2022). PDC*lung01 was shown to expand antitumor CD8+ T-cells from HLA-A*02:01+ PBMC of patients with melanoma or NSCLC and to be synergistic with anti-Programmed Cell Death (PD)-1 (Pembrolizumab; Charles, OncoImmunol 2020; Lenogue, Vaccines 2021; Hannani, Int. J. Mol. Sci. 2023). PDC*lung01 was immunogenic and had a manageable safety profile in all cohorts and show promising clinical activity when combined with anti-PD-1 in metastatic NSCLC (Vansteenkiste, ELCC 2025).



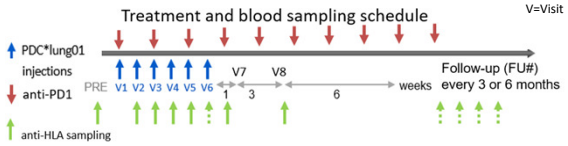
- **DSA** (Donor Specific antibodies); antibodies against to HLA molecules expressed by PDC* line cells were assessed during treatment (humoral allogeneic response)

PDC-LUNG-101 study design (NCT03970746)

	Cohort	Arm	# of patients	NSCLC Patient Criteria	Main Objectives
Phase I	PDC*lung01 Mono — A1 Low dose	2M cells/peptide	6	• Stage IIa/IIb/IIIa after R0 resection • Adjuvant chemotherapy +/- radiotherapy	• Safety & tolerability • Immune activity
	PDC*lung01 Mono — A2 High dose	20M cells/peptide	10		
Phase II	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%)	• Dose range • Clinical activity: - Overall Response Rate (ORR) - Median Progression Free Survival (mPFS) - Disease Control Rate (DCR)
	Anti-PD-1 + PDC*lung01 — B2 High dose	20M cells/peptide + anti-PD-1	45		

PDC*lung01 administration schedule: IV+SC every week X 6 times

Anti-PD-1 administration schedule: IV, every 3 weeks (until progression)

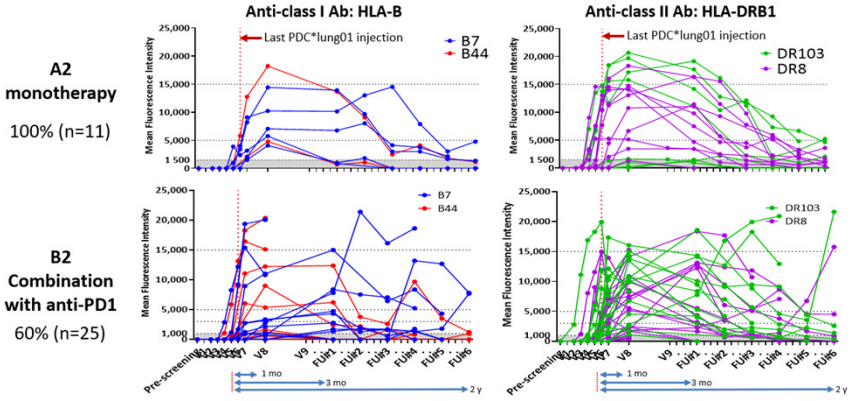


- **PDC*line cells express both HLA class I and class II molecules**

HLA class I: **HLA-A*02:01; HLA-B*07:02; HLA-B*44:02,** HLA-C*05:01, HLA-C*07:02

HLA class II: **HLA-DRB1*01:03; HLA-DRB1*08:01**; HLA-DQB1*04:02, HLA-DQB1*05:01; HLA-DPB1*02:01; HLA-DPB1*04:01, HLA-DPA*01:03

DSA are similarly generated both in patients treated by PDC*lung01 in monotherapy or in combination with anti-PD1 (High dose)

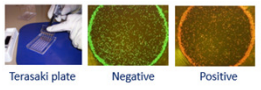


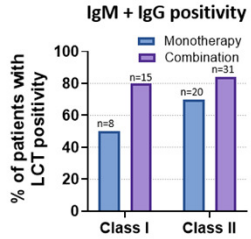
LIFECODES LifeScreen Delux & LSA (Immucor/Werfen)

- Only one patient in low dose cohorts generated anti-HLA antibodies (1 out of 12: 8.3%)
- No clinical side effect was associated to the presence of anti-HLA Ab

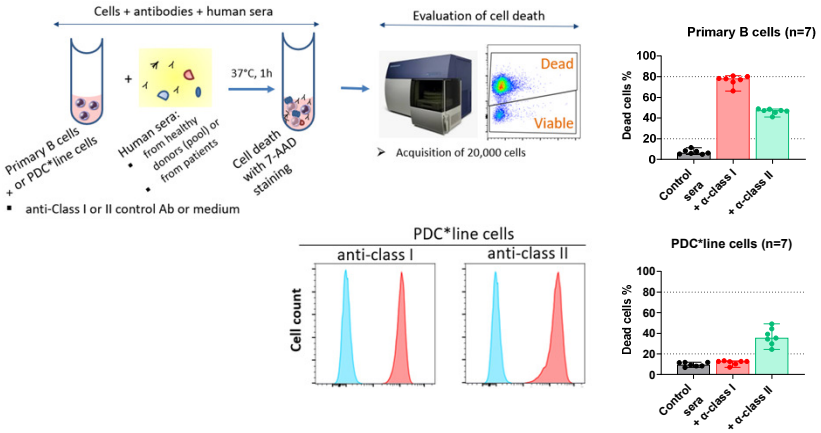
The function and the nature of DSA are similar in patients treated by PDC*lung01 in monotherapy or in combination with anti-PD1

- Lymphocytotoxicity assay
  - 2 samples per patient at the immunization peak
  - with or without DTT
  - with one donor's cells per specificity
    - B7 or B44 positive T-cells
    - DR103 or DR8 positive B cells
- Antibody-mediated complement dependent cytotoxicity (CDC) observed with anti-class I & anti-class II molecules
- Lot of DSA are IgM (57%)

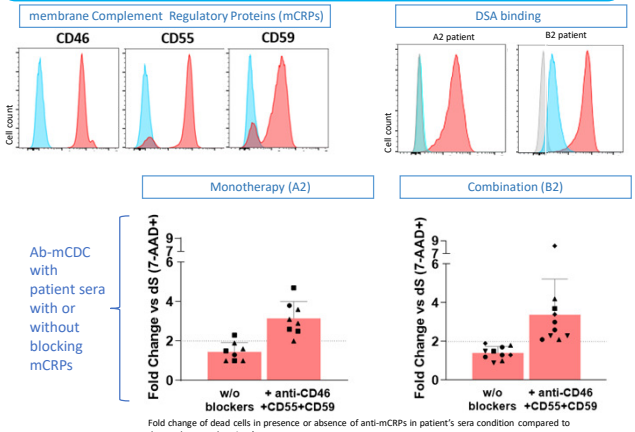




PDC*line cells are resistant to antibody-mediated CDC (Ab-mCDC) in a cell cytotoxic assay using human sera and flow cytometry



PDC*line cells express membrane Complement Regulatory Proteins (mCRPs) allowing resistance to Ab-mCDC



Fold change of dead cells in presence or absence of anti-mCRPs in patient's sera condition compared to decomplemented patient's sera

Conclusion

- Altogether, this study shows the innocuity and the absence of deleterious effect of anti-HLA Ab on allogeneic PDC*line cells used as a cancer vaccine platform. Importantly, anti-HLA generation is dose dependent and anti-PD1 treatment does not seem to modify the nature, the functionality and the dynamics of anti-HLA IgG response.

Protocol Nb: PDC-LUNG-101, Status: Recruitment completed, Clinical Trial Identification: NCT03970746; This study is sponsored by PDC*line Pharma SAS. Contact info: j.plumas@pdc-line-pharma.com