A New Plasmacytoid Dendritic Cell-Based Vaccine in Combination with Anti-PD-1 Expands Tumor-Specific CD8+ T Cells of Lung Cancer Patients

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49th Annual Meeting of Korean Cancer Association
& 9th International Cancer Conference

OFF-THE-SHELF ALLOGENEIC PLASMACYTOID DENDRITIC CELL-BASED CANCER VACCINE

PDC line

Human PDC leukemia origin cell line

Growth in bioreactor in suspension in synthetic medium

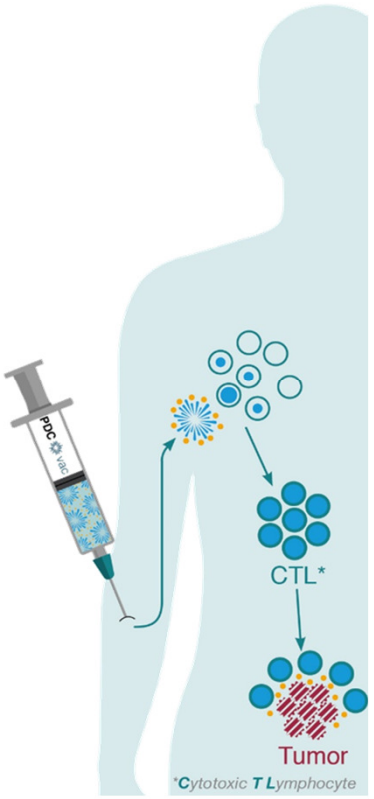
PDC vac

Pulsed with tumor peptides

Irradiation
(Proliferation stopped, functionality conserved)

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH



Priming of cytotoxic anti tumor CD8+ T-cell (CTL) in Lymph Nodes

Expansion following boost -ing by PDC*vac and trafficking in bloodstream

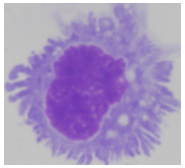
Migration to tumor bed and killing of tumor cells

Plumas, Current Opinion Oncology, 2022

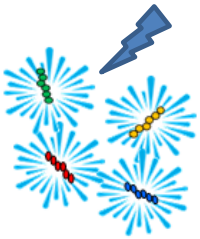
OFF-THE-SELF ALLOGENEIC DENDRITIC-CELL BASED VACCINES ARE ATTRACTIVE FOR MANY REASONS

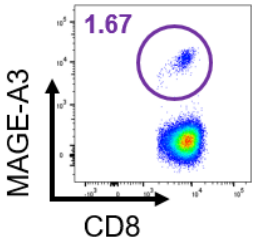
- Allogeneic cancer vaccines can be easily manufactured as the cell source is independent from patients
- The drug product is immediately available for the patients upon enrolment
- The use of the same product guarantees the homogeneity of the treatment and the homogeneity of clinical results
- Its potency to stimulate antitumor CD8 T-cells can be checked before infusion
- The manufacturing process is cost-effective and scalable
- DC directly stimulate naïve or memory antigen-specific T-cells in lymphoid organs or tissues

PDC*VAC CAN PRIME AND EXPAND NAÏVE ANTIGEN-SPECIFIC T-CELLS IN VITRO AND IN VIVO



Human peptide-loaded PDC*line

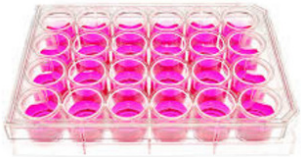




Human tumor specific CD8+ T cells

Proof of concept with HUMAN material

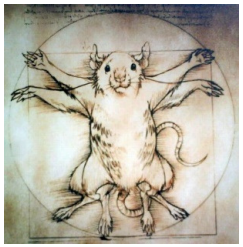
Human Mononuclear cells



heathy donor's
cord or venous blood
patient's venous blood
(melanoma, NSCLC)

Lenogue, Vaccine, 2021
Aspord, 2010, 2011, 2012

Humanized mice



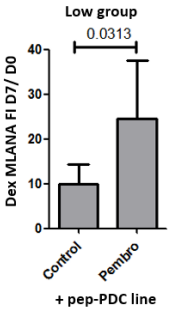
Hu_{PBMC}NOD-Scid ß2m^{ko}
Hu_{CD34+}NOG/NSG

Plumas, Current Opinion Oncology, 2022

First-in-man clinical trial

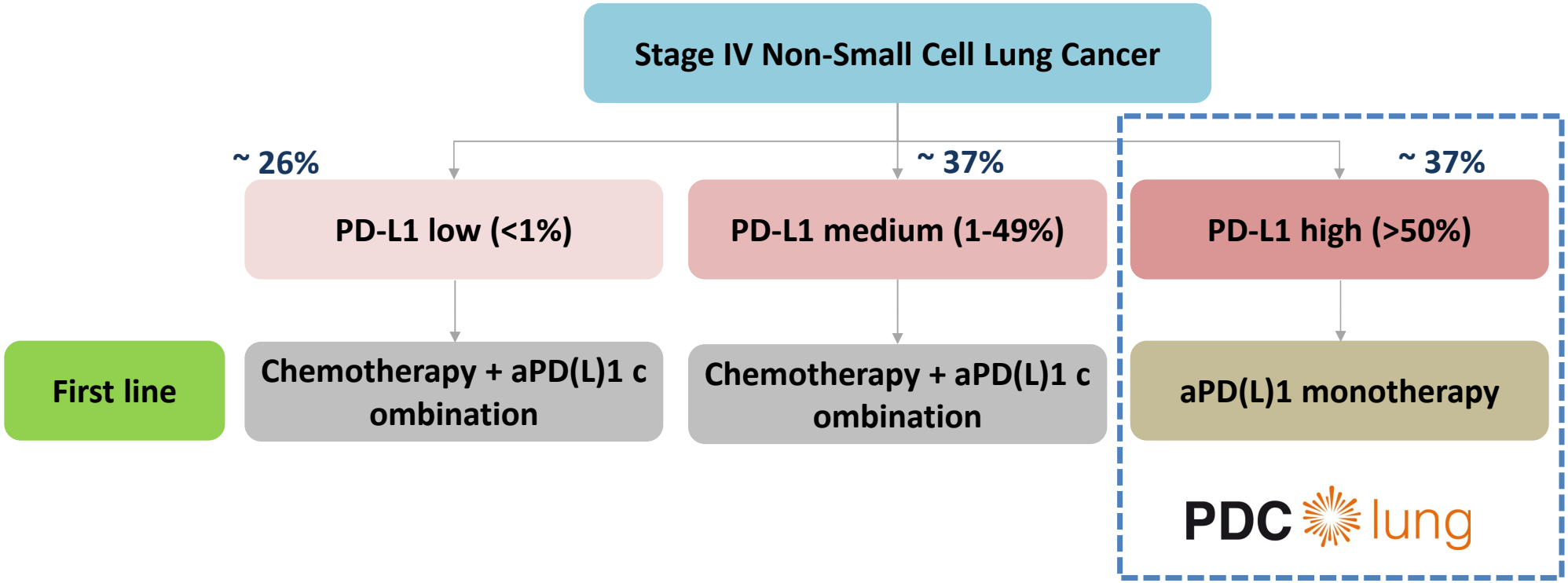
Melanoma patients

Ex-vivo



Charles, OncoImmunology, 2020

POSITIONING OF PDC*LUNG FOR ADVANCED STAGE NSCLC



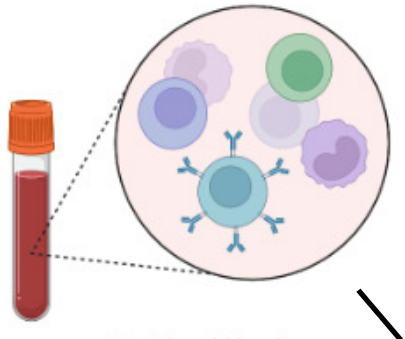
PATIENTS AND TUMOR ASSOCIATED ANTIGENS

- **34 PBMCs from NSCLC patients**
  - 9 females, 25 males
  - Median age: 61.5 y
  - 22 AC, 8 SCC, 4 others
  - Stage I (11); II (13); IIIA (7)
  - Smoking status: A (20), F (11), NS (2)
- **14 peptides derived from tumor antigens**
  - CGA: 9
  - Over: 4
  - Post-T: 1
- **Cocultures with PDC*line cells loaded with a maximum of 6 TAA**

Hannani, Int J Med Sci 2023

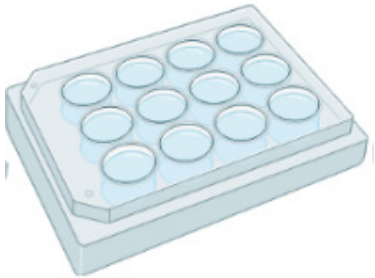
Antigen Type	Antigen	Peptide Sequence (HLA-A*02:01)	References of immunogenicity discovery
Cancer-Germline Antigens (CGA)	MAGE-A1	$_{278}$KVLEYVIKV$_{286}$	(Ottaviani et al., 2005; Pascolo et al., 2001)
	MAGE-A2	$_{157}$YLQLVFGIEV$_{166}$	(Kawashima et al., 1998)
	MAGE-A3.1	$_{112}$KVAELVHFL$_{120}$	(Kawashima et al., 1998)
	MAGE-A3.2	$_{271}$FLWGPRALV$_{279}$	(van der Bruggen et al., 1994)
	MAGE-A4	$_{230}$GVYDGREHTV$_{239}$	(Duffour et al., 1999)
	MAGE-A9	$_{223}$ALSVMGVYV$_{231}$	(Oehlrich et al., 2005)
	MAGE-A10	$_{254}$GLYDGMEHL$_{262}$	(Huang et al., 1999)
	NY-ESO-1 (CTAG1B)	$_{157}$SLLMWITQC$_{165}$	(Chen et al., 2000; Jäger et al., 1998; Valmori et al., 2000)
	CAMEL (CTAG2)	$_{152}$MLMAQEALAFL$_{162}$	(Aarnoudse et al., 1999)
Overexpressed Antigens	GLULD1 (LGSN)	$_{270}$FLPEFGISSA$_{279}$	(Nakatsugawa et al., 2011)
	SURVIVIN (BIRC5)	$_{95}$ELTLGEFLKL$_{104}$	(Schmidt et al., 2003; Schmitz et al., 2000)
	HER2 (ERBB2)	$_{369}$KIFGSLAFL$_{377}$	(Fisk et al., 1995)
	WT-1	$_{126}$RMFPNAPYL$_{134}$	(Oka et al., 2000)
Post-translational	MUC-1	$_{12}$LLLLTVLTV$_{20}$	(Brossart et al., 1999)

EXPANSION OF ANTIGEN-SPECIFIC T-CELLS WITH PEPTIDE-LOADED PDC*LINE CELLS



Patient's PBMCs

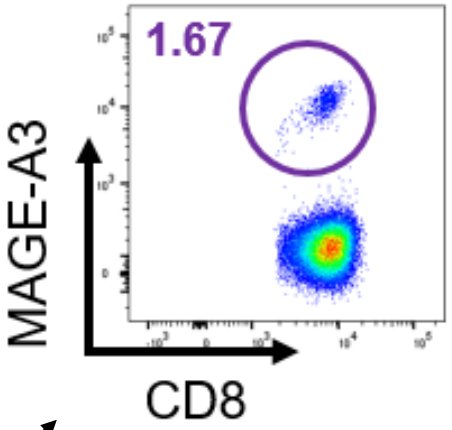
peptide-loaded PDC*line cells



Coculture with IL2

14d to 21d

Harvest



Flow cytometry

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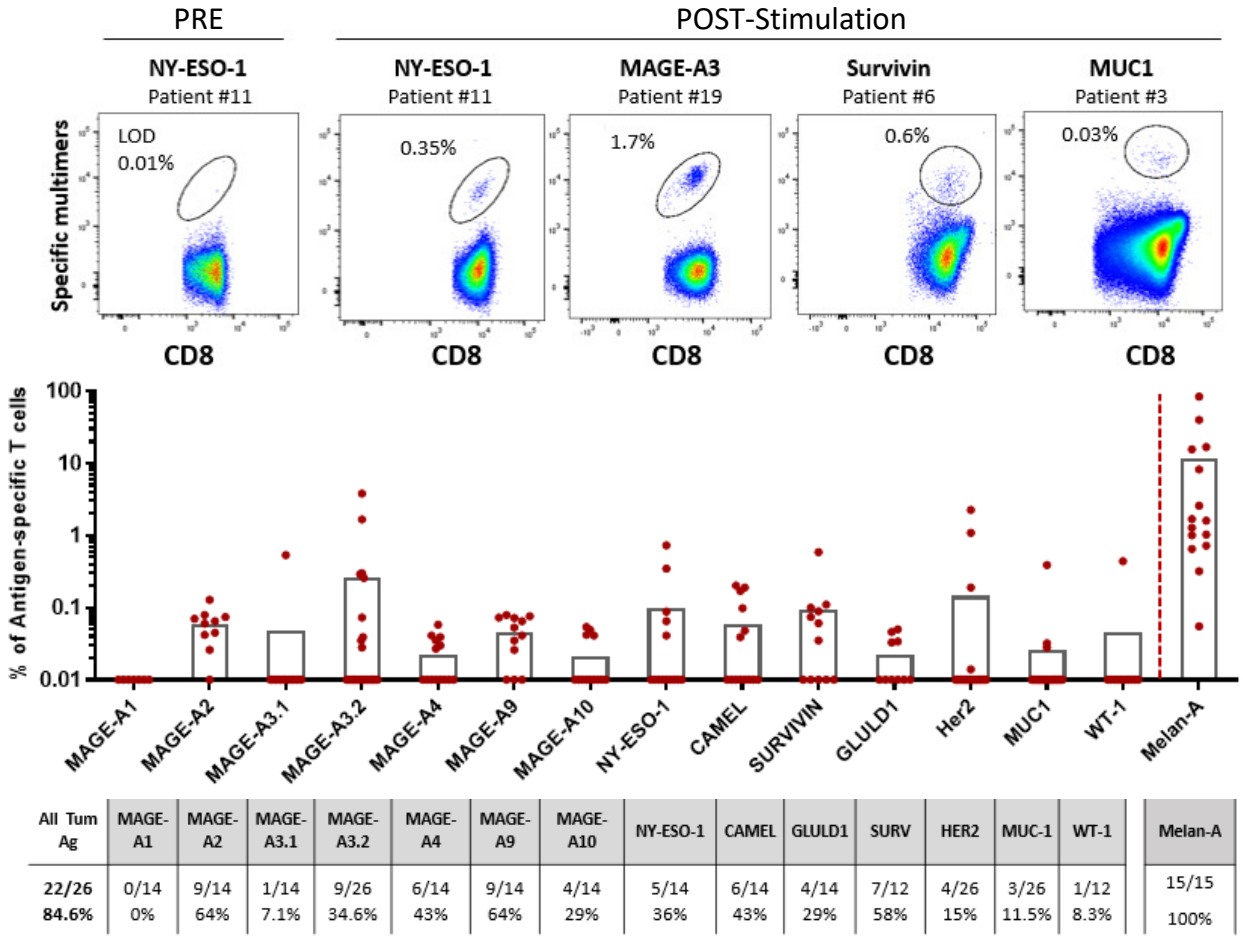
PDC*LINE CELLS INDUCE A BROAD ANTITUMOR RESPONSE IN LUNG CANCER PATIENTS



All Tum Ag	MAGE-A1	MAGE-A2	MAGE-A3.1	MAGE-A3.2	MAGE-A4	MAGE-A9	MAGE-A10	NY-ESO-1	CAMEL	GLULD1	SURV	HER2	MUC-1	WT-1	Melan-A
22/26	0/14	9/14	1/14	9/26	6/14	9/14	4/14	5/14	6/14	4/14	7/12	4/26	3/26	1/12	15/15
84.6%	0%	64%	7.1%	34.6%	43%	64%	29%	36%	43%	29%	58%	15%	11.5%	8.3%	100%

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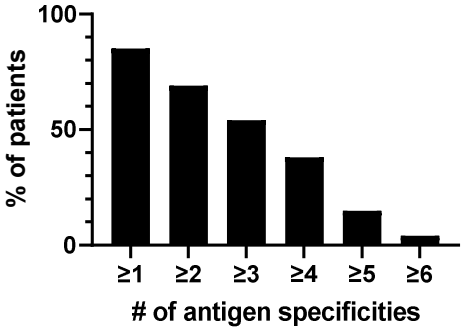
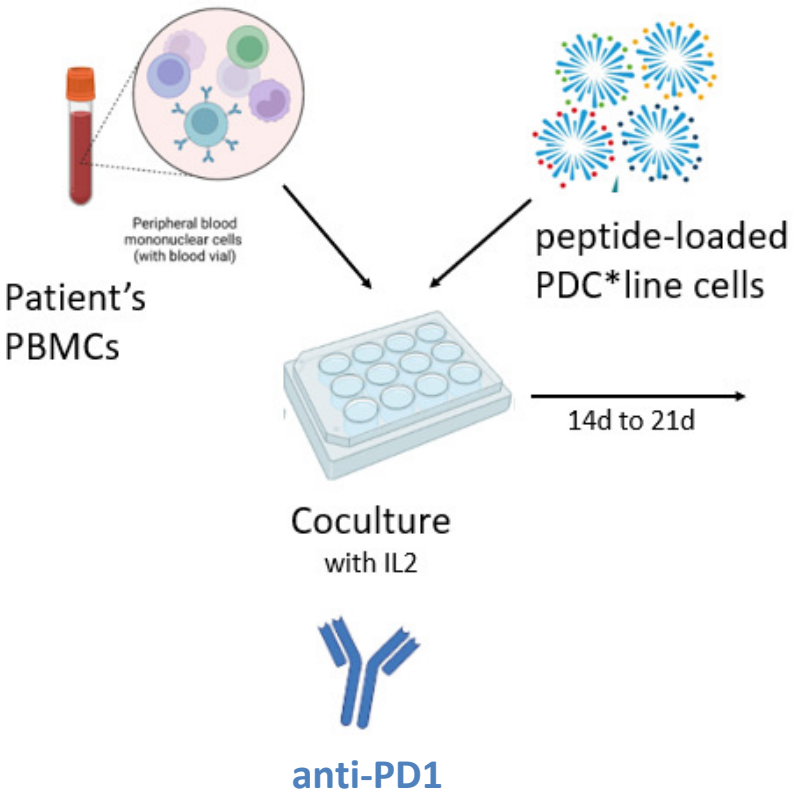
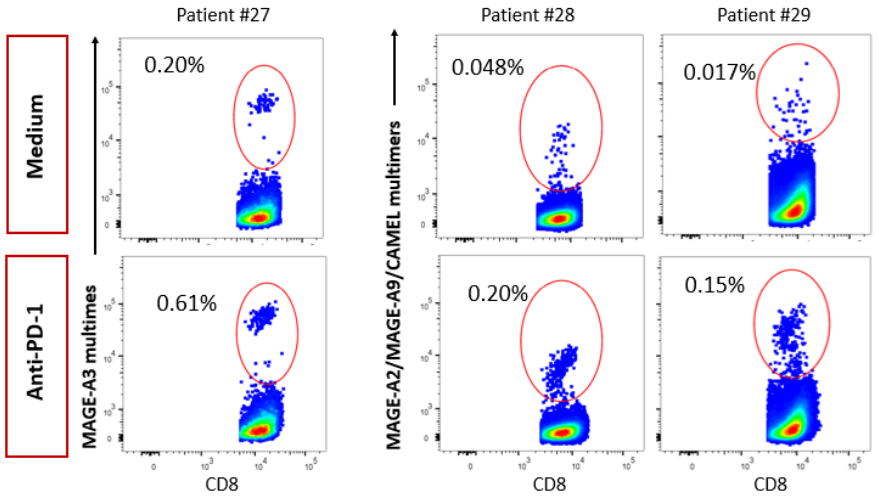
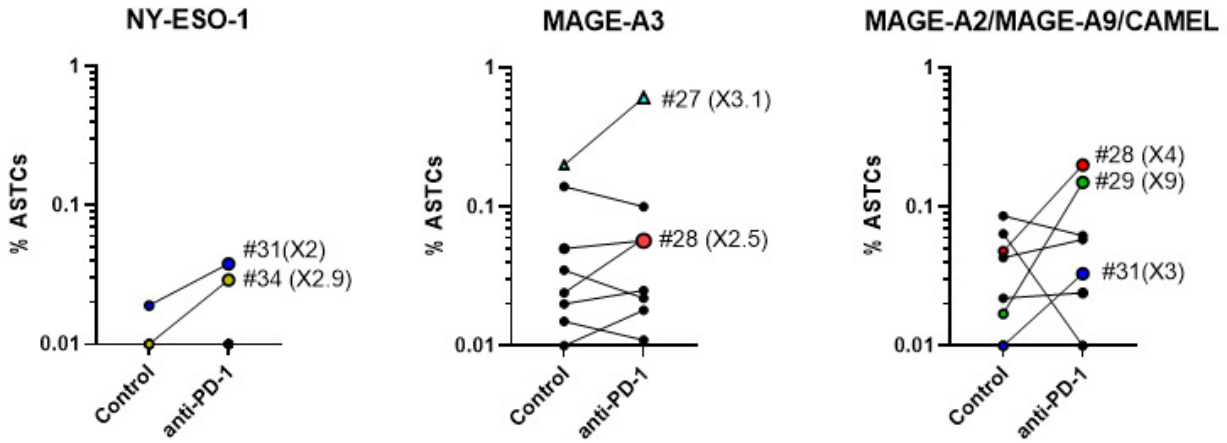


- 85% of patients ≥ 1 TAA
- 69% of patients ≥ 2 TAA
- 39% of patients ≥ 4 TAA

ANTI-PD1 SYNERGIZES WITH PEPTIDE-LOADED PDC*LINE CELLS TO EXPAND ANTITUMOR CD8+ T CELLS







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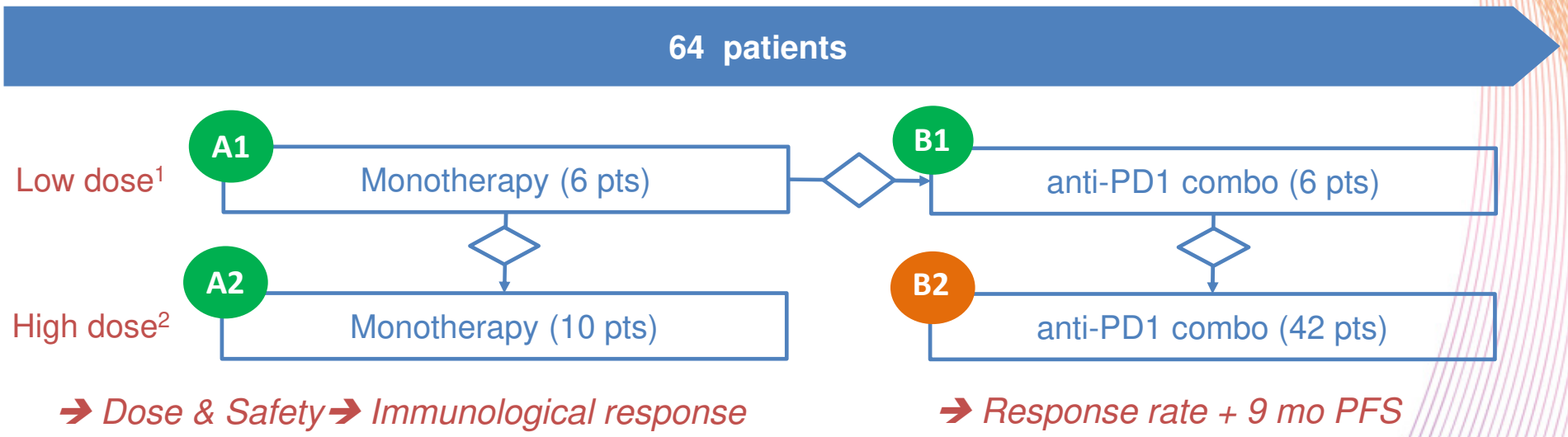
TAKE HOME MESSAGES

- PDC*line cells are very potent to prime and expand antigen-specific CD8+ T-cells
- PDC*vac platform allows the expansion of antitumor CD8+ T-cells in a large proportion of lung cancer patients whatever the stage and the histological type of the disease
- Combination of anti-PD1 and PDC*line cells significantly improves the immune response in lung cancer patients, as we have seen in melanoma patients
- Based on this preclinical proof-of-concept, the PDC*vac platform is currently being evaluated in combination with Pembrolizumab in NSCLC (trial number NCT03970746).

PDC-LUNG-101: DESIGN & OBJECTIVES (NCT03970746)

PHASE I/II : safety, immunological activity and Clinical response of PDC*lung01 +/- anti-PD-1



➔ *Dose & Safety* ➔ *Immunological response* ➔ *Response rate + 9 mo PFS*

A patients : Maintenance setting: Stage IIa/IIb/IIIa following surgery, adjuvant chemotherapy +/- radiotherapy

B patients : First line: Stage IV with TPS>50%

PDC*lung tested doses:
[1]Low Dose: 2 million cells / peptide
[2]High Dose: 20 million cells / peptide

PDC*lung administration schedule :
Prime/repeat boosts protocol : IV+SC
every week x 6 (phase I/II)

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

THANK YOU FOR YOUR KEEN INTEREST

PDC*line Pharma SA, Headquarter

PDC*line Pharma SAS, subsidiary

PDC*line Pharma Seoul Office

www.pdc-line-pharma.com