An open-label, dose-escalation, phase I/II study to assess the safety, the tolerability, the immunogenicity and the preliminary clinical activity of the therapeutic cancer vaccine, PDC*lung01, associated or not with anti-PD-1 treatment in patients with non-small-cell lung cancer (NSCLC)

Published: 11-03-2021
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This study has been transitioned to CTIS with ID 2024-517429-24-00 check the CTIS register for the current data. Objectives:Primary:- Assess safety and tolerability of PDC*lung01 vaccinations administered at two dose levels as single agent or during...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON56303

Source
ToetsingOnline

Brief title
Safety, immunogenicity & clinical activity study of PDC*lung01 in NSCLC

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
lung cancer, NSCLC

Research involving
Human

Sponsors and support

Primary sponsor: PDC*line Pharma SAS
Source(s) of monetary or material Support: PDC*line Pharma SAS

Intervention

Keyword: anti-PD-1, dendritic, NSCLC, vaccine

Outcome measures

Primary outcome

Primary endpoint: Occurrence of dose-limiting toxicities (DLT) related to the administration of PDC*lung01.

Secondary outcome

Secondary endpoint:

- Occurrence of serious adverse events (SAEs) and adverse events (AEs), deemed as related to the association of PDC*lung01 and the anti-PD-1 therapy, monitored during study treatment until daysafter the last dose of PDC*lung01 (cohorts A and B) and 21 days after the last dose of PDC*lung01 (Cohort C1).
- Occurrence of serious adverse events (SAEs) and adverse events (AEs), monitored during study treatment until 28 days after the last dose of PDC*lung01 (cohorts A and B) and 21 days after the last dose of PDC*lung01 (Cohort C1).
- Measurement of anti-HLA class I and II antibodies in the serum. In case of positive detection, the allelic specificity of the antibodies will be

determined.

- Ex vivo detection and characterization of CD8+ T cells against tumor antigens

borne by PDC*lung01, using flow cytometry.

- Objective Response Rate (according to RECIST version 1.1) for cohorts B2 and

C1

- Objective Response Rate (according to iRECIST) for cohorts B2 and C1

- Progression-Free Survival at 9 months according to RECIST 1.1 and according

to iRECIST from the first day of anti-PD-1 antibody administration for cohorts

B2 and C1

Study description

Background summary

PDC*vac is a therapeutic cancer vaccine product based on the PDC*line, irradiated and loaded with target tumor peptides to prime and expand antitumor T cells. PDC*line being homozygote for HLA-A*02:01 allele, peptides loaded on this specific APC are HLA-A*02:01 restricted.

PDC*line Pharma has demonstrated PDC*vac efficiency and potency to prime and expand tumor-specific cytotoxic T cells, specific for different tumor antigens, including neoantigens, from different sources of human mononuclear cells, including cells from cancer patients, in
vitro and in vivo in humanized mouse models.
PDC*vac currently comes in two cancer investigational drugs: PDC*mel (also called GeniusVac-Mel4), developed for melanoma and PDC*lung01 for non-small cell lung cancer (NSCLC).

Anti-PD-1 antibodies have recently become first-line standard-of-care treatments of melanoma and NSCLC. However, PD-L1 or PD-1 inhibition is not sufficient for optimum anti-tumor activity in some patients. Therefore, strategies to boost naïve and memory CD8 T cell immune response against tumor antigens represent a unique possible approach to potentiate the efficacy of immune check point inhibitors and particularly of anti-PD-1.
The potential synergy between peptide-loaded PDC*line cells and anti-PD-1 antibody in expanding antigen specific T cells has therefore been investigated

ex vivo with patient*s cells and results clearly showed that anti-PD-1 strongly synergizes with peptide-loaded PDC*line and triggers
potent amplification of tumor-specific CD8+ T cells from cancer patients.

Study objective

This study has been transitioned to CTIS with ID 2024-517429-24-00 check the CTIS register for the current data.

Objectives:
Primary:
- Assess safety and tolerability of PDC*lung01 vaccinations administered at two dose levels as single agent or during maintenance treatment by pemetrexed (for adenocarcinomas in Cohorts A1 and A2) or during treatment with anti-PD-1 therapy (Cohorts B1, B2 and C1).
Secondary:
- Evaluate the safety of the combined use of PDC*lung01 with anti-PD-1 therapy;
- Document additional indicators of safety / tolerability;
- Evaluate the humoral allogeneic immune response against PDC*line cells;
- Evaluate the specific T-cell response against the antigens borne by PDC*lung01 vaccine; and
- Document preliminary clinical activity.

Study design

Open-label, multicenter, dose-escalation, phase I/II study

Approximately 70 evaluable patients planned to be included in the following 4 cohorts:
A1 (LD): 14 x 10^6 cells PDC*lung01
A2 (HD): 140 x 10^6 cells PDC*lung01
B1 (LD): 14 x 10^6 cells PDC*lung01 + anti-PD-1
B2 (HD): 140 x 10^6 cells PDC*lung01 + anti-PD-1
C1 (HD+Boost): 140 x 10^6 cells PDC*lung01 + anti-PD-1 and 70 x 10^6 cells PDC*lung01 + anti-PD-1

Intervention

Test product: PDC*lung01 includes, in similar proportion, seven active agents, made of irradiated human plasmacytoid dendritic cells (PDC) loaded separately with a distinct synthetic peptide encoded by a lung tumor antigen, namely NY-ESO-1, MAGE-A3, MAGEA4, Multi-MAGE (an epitope common to several MAGE-A antigens), SURVIVIN, MUC1 or a peptide derived from the Melan-A antigen.

Doses: 14 x 10^6 (LD) or 140 x 10^6(HD) cells per administration, split equally (2 x 1,5ml) for two injection routes (IV and SC), 6 administrations one week

apart. In addition to the HD administrations, the C1 cohort will receive booster administrations with 70 x 10^6 (HD) cells per administration, 1,5ml , 6 administrations three weeks apart.

Two consecutive administrations: subcutaneous followed by intravenous. Booster administrations will only include intravenous injections.

Duration of treatment: planned for 6 weeks, 25 weeks for Cohort C1

Study burden and risks

Burden/risks:
The currently known risks are:
• Skin reactions at the injection site: erythema, redness, hardening and swelling after the injection.
• Furthermore, as with traditional vaccinations, local reactions may include: pain in the area of the injection site, muscle pain, tenderness, vitiligo (pigmentary skin reaction) and itching.
• Reactions associated with the administration of vaccines: tiredness, faintness, headache and/or fever.
This will be the first time PDC*lung01 is administered in humans. During previous studies, conducted by other research teams on anticancer immunotherapy treatments containing dendritic cells, minor events such as injection site reactions, tiredness, muscle pain and headache were observed. A medicinal product under development that is similar to PDC*lung01 but developed to treat melanoma, was subcutaneously administered to participants. Most of the side effects were temporary skin reactions.

Expected benefit:
The aim of PDC*lung01 treatment is to prime and boost patients* CD8 T cells specific for tumor antigens, and by doing that to potentiate the efficacy (prolongation of reponse rate and progression free survival) of immune check point inhibitors and particularly of anti-PD-1.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Pre-screening: Documented HLA-A*02:01 positivity and absence of anti-HLA antibodies against HLA molecules expressed by the PDC*line, after the patient has provided written informed consent.. Screening: 1.Patients with histologically proven, or cytologically proven, non-small-cell lung cancer (NSCLC). The stage of the disease is evaluated according to the classification of the American Joint Committee on Cancer, 8th edition. a.For the dose-escalation phase (Cohorts A1 and A2): (i)Stage IIa/IIb/IIIa NSCLC following radical surgery (R0 resection) and, if applicable, adjuvant platinum-based chemotherapy, or (ii)Stage IV histologically or cytologically confirmed case of epidermoid (squamous) lung cancer following 4 cycles of platinum-based therapy, if targeted treatment options were not indicated,or (iii)Stage IV histologically or cytologically confirmed case of adenocarcinoma (non-squamous) lung cancer following 4 to 6 cycles of pemetrexed and platinum combination, if targeted treatment options were not indicated, (iv)Populations (ii) and (iii) who have stopped prematurely chemotherapy, after at least 2 cycles of platinum-based therapy, for any reason, AND do present with a documented stable disease or partial / complete response. b.For the anti-PD-1 immunotherapy (Cohorts B1, B2 and C1): -The patient has first-line metastatic stage IV NSCLC measurable disease and is starting anti-PD-1. The intention and decision to prescribe the anti-PD-1 monotherapy as SoC (TPS>=50%), assuming no targeted mutation detected, following standard NGS testing, if applicable, and thus no targeted treatment option is indicated, must have been made by the investigator before and regardless of the patient's participation in the study. Radiotherapy/chemoradiotherapy for prior stage III NSCLC is allowed if the

treatment-free interval is >1 year. 2.ECOG performance status 0 or 1. 3.Adequate renal and hepatic function as defined below: •Serum creatinine clearance > 50 mL/min (Cockcroft-Gault formula) •Bilirubin <= 1.5 times upper limit of normal (ULN) •Aspartate transaminase (AST) and alanine transaminase (ALT) <= 2.5 times ULN (up to 5 times ULN are allowed in case of presence of liver metastases). 4.Adequate haematological function as defined below: •Platelet count >= 70x10^9 /L; •White blood cell count >= 2.5 x 10^9 /L with •lymphocytes >=1x10^9 /L at screening or at baseline , and •absolute neutrophil count >=1.5x10^9/L, •Haemoglobin >= 90 g/L 5.Patient willing to provide a baseline blood sample for leucocyte enumeration, cellular allogeneic response and immune-monitoring of 100 ml in total (in one or two samplings). 6.For patients with brain metastases: •Central nervous system metastases are not symptomatic or have been treated, •Subjects with symptomatic CNS metastases must be either off corticosteroids, or on a stable or decreasing dose of <=10mg daily prednisone (or equivalent) during at least 2 weeks before baseline. 7.For female patients without child-bearing potential: a documentation of tubal ligation or hysterectomy, ovariectomy or a post-menopausal status is available. For female patients of child-bearing potential: a negative serum pregnancy test at screening is provided. The patient agrees to use a highly effective contraception method from signing informed consent form (screening), throughout the study treatment period with PDC*lung01 and for at least 28 days after the last administration of PDC*lung01. For female patients receiving Pemetrexed in cohorts A1/A2 concomitantly with PDC*lung01, according to corresponding SmPC, it is required to use effective contraception during treatment with pemetrexed. For female patients receiving Pembrolizumab in cohorts B1/B2/C1 concomitantly with PDC*lung01, according to corresponding SmPC, it is required to use an effective method of contraception up to 4 months thereafter. 8. Males with reproductive potential should use barrier method of contraception (condom) from signing informed consent form (screening) up to at least 28 days after the last dose of PDC*lung01. For male patients receiving Pemetrexed in cohorts A1/A2 concomitantly with PDC*lung01, according to corresponding SmPC, it is required to use barrier method of contraception up to 6 months thereafter. 9. In the Investigator*s opinion, the patient is able and willing to comply with the requirements of the study. 10. Patient willing and able to sign the study informed consent form before any study-specific procedures are conducted. 11. Patient (male or female) is aged 18 years or above.

Exclusion criteria

1.Mixed small-cell and non-small-cell histological features. 2.Patient has previously documented evidence of EGFR mutation, ALK fusion or ROS1 fusion (according to current ESMO clinical practice guidelines) or any mutation for which targeted treatment options would be indicated, as per SoC. 3.Patient has received immunotherapy or any investigational drugs within 4 weeks before the first PDC*lung01 dose. Chemoradiotherapy with consolidation durvalumab for

prior stage III disease. 4. Patient with Stage IV disease that received prior radiotherapy (except palliative radiotherapy e.g. brain irradiation). Palliative radiotherapy for stage IV disease should be completed one week prior to baseline visit and for brain irradiation a 2-week window is required. 5.Patient without brain metastasis is receiving systemic corticosteroids at a dose level exceeding 10 mg/day (prednisone or equivalent) during the screening period (administration by nasal spray, topical solution or oral inhaler is non-systemic and is therefore allowed). 6.Patient has a medical history of cancer other than NSCLC, except the following: (i) non-melanoma skin cancer with complete resection, (ii) adequately treated carcinoma in situ, (iii) other cancer treated with no evidence of disease for at least five years with the exception of pT1-2 prostatic cancer Gleason score < 6 and superficial bladder cancer. 7.Known hepatitis B and/or C infection (testing not required). 8.Known positive for human immunodeficiency virus (HIV; testing not required). 9.Uncontrolled congestive heart failure or hypertension, unstable heart disease (coronary artery disease with unstable angina or myocardial infarction within 6 months of baseline) or uncontrolled ventricular arrhythmias at the time of enrolment in the study (atrial fibrillation or flutter is acceptable). 10.Any history of splenectomy or splenic irradiation. 11.For female patients: pregnancy or lactation. 12.Any condition, including autoimmune or immunodeficiency active disease that, in the opinion of the Investigator, would jeopardise patient*s safety, or might compromise the effect of the study drug or the assessment of the study result. Patients with vitiligo, diabetes Type I, psoriasis (not requiring psoralen plus ultraviolet A radiation, methotrexate, retinoids, or oral corticosteroids within the previous 12 months) or a history of autoimmune thyroiditis are not excluded.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting

Start date (anticipated):	16-11-2021
Enrollment:	11
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Generic name:	Somatic cels allogenic
Product type:	Medicine
Brand name:	ALIMTA
Generic name:	Pemetrexed
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	KEYTRUDA
Generic name:	Pembrolizumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	PDC*lung01
Generic name:	PDC*lung01

Ethics review

Approved WMO Date:	11-03-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-05-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-07-2021
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-08-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-11-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-11-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-07-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-07-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	31-03-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-07-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO	

Date:	14-07-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	04-09-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-11-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	04-12-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2024-517429-24-00
EudraCT	EUCTR2018-002382-19-NL
ClinicalTrials.gov	NCT03970746

Register	ID
CCMO	NL76134.000.21