Protocol PDC-LUNG-101

Safety, Immunogenicity and Preliminary Clinical Activity Study of PDC*lung01 Cancer Vaccine in NSCLC

This is the trial summary as assessed on clinicaltrials.gov on 06/06/2019.

Minor changes in the protocol may occur. You can check this on this direct link: https://clinicaltrials.gov/ct2/show/NCT03970746?cond=Lung+Cancer&cntry=BE&city=Leuven&rank=7

Trial Design:

PDC-LUNG-101 trial is 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 NSCLC.

Detailed Description:

The therapeutic cancer vaccine, PDC*lung01 will be administered at two dose levels (low dose (LD) and high dose (HD)), as single agent or during maintenance treatment by pemetrexed (for adenocarcinomas in Cohorts A1 and A2) or added to the SoC (cohorts B1 and B2) i.e. anti-PD-1.

In cohorts A1 (low dose cohort) and A2 (high dose cohort), NSCLC patients will be treated at each of the six PDC*lung01 treatment visits with low dose/high dose administered successively by subcutaneous and then by intravenous route.

In cohort B1 and B2, the first PDC*lung01 injection will start within 48 hours after the first infusion of anti-PD-1. The fourth PDC*lung01 injection will occur within 48 hours after the infusion of the second cycle of anti-PD-1.

For each patient, the study will be divided into three consecutive parts:

Pre-screening (for HLA-A*02:01 positivity), only patients with positive HLA-A*02:01 status will be proposed to be screened.

Active period comprising a screening period, a treatment period (visits V1 to V6, during which the patient receives PDC*lung01 vaccine, at each visit) and an end-of-treatment (EoT) visit (V7, 4 weeks after the last injection),

Follow-up period which starts after the EoT visit and lasts up to two years after the first IMP administration.

Inclusion Criteria:

Pre-screening:

Documented HLA-A*02:01 positivity after the patient has provided written informed consent.

Only patients showing a documented positive result in pre-screening will be allowed to enter the screening period.

Screening:

1. Patients with histologically proven, or cytologically proven (allowed only for patients recruited in cohorts A1/A2), NSCLC. The stage of the disease is evaluated according to the classification of the American Joint Committee on Cancer, 8th edition (see Section 25.1)

   a. For the dose-escalation phase (Cohorts A1 and A2): a wash-out period of at least 4 weeks after administration of the last cycle of platinum-based chemotherapy is required.

   (i) Stage IIa/IIb/IIIa NSCLC following surgery and, if applicable, following adjuvant platinum-based chemotherapy, or (ii) Stage IV histologically or cytologically confirmed case of epidermoid (squamous) NSCLC following 4 courses of platinum-based therapy, or (iii) Stage IV histologically or cytologically confirmed case of adenocarcinoma (non-squamous) lung cancer NSCLC following 4 to 6 courses cycles of pemetrexed and platinum combination, (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 complete response.

   b. For the anti-PD-1 immunotherapy (Cohorts B1 and B2):

   - The patient has first-line metastatic stage IV NSCLC disease and is starting anti-PD-1. The intention and decision to prescribe the anti-PD-1 monotherapy as SoC (TPS≥50%) must have been made by the investigator before and regardless of the patient's participation in the study.

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 ≥ 70 x 10^9/L;
- White blood cell count ≥ 2.5 x 10^9/L with

- lymphocytes ≥ 1 x 10^9/L, among which ≥ 10 % of CD8+ T cells and
- absolute neutrophil count ≥ 1.5 x 10^9/L;
- Haemoglobin ≥ 90 g/L

5. Patient willing and able 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 and have been treated,
- In addition, subjects 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 required. The patient agrees to practice a "dual method" contraception 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 concomitantly with PDC*lung01, according to corresponding SmPC, it is required to use an effective method of contraception up to 4 months thereafter.

   A woman is considered of childbearing potential (WOCBP), i.e. fertile, following menarche and until becoming post-menopausal unless permanently sterile. Permanent sterilisation methods include hysterectomy, bilateral salpingectomy and bilateral oophorectomy.

   A postmenopausal state is defined as no menses for 12 months without an alternative medical cause.

   "Dual method" contraception is defined as the use of at least 2 methods among the following:

- Hormonal contraception (such as oral, injection, transdermal patch, implant)
- Barrier (condom with spermicide or diaphragm with spermicide) during intercourse
- Intrauterine device
- Monogamous relationship with vasectomized partner.
- Abstinence or absence of sexual relations

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 (Cohorts B1 and B2). If unable to provide documentation of these molecular changes, an archival formalin-fixed paraffin-embedded tumour tissue should be submitted for testing.
3. Patient has received immunotherapy or any investigational drugs within 4 weeks before the first PDC*lung01 dose.
4. Patient without brain metastases has been receiving systemic corticosteroids at any dose for a period longer than 10 days before baseline (administration by nasal spray, topical solution or oral inhaler is non-systemic and is therefore allowed).
5. Patient has a medical history of cancer other than NSCLC, except the following: (i) non-melanoma skin cancer with complete resection, (ii) in situ carcinoma of the cervix, (iii) other cancer treated with no evidence of disease for at least five years.
6. Patient presents at screening anti-HLA antibodies against HLA molecules expressed by the PDC*line.
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.