AN OPEN-LABEL, PHASE I STUDY OF NEO-PTC-01 IN PATIENTS WITH ADVANCED OR METASTATIC MELANOMA

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This study has been transitioned to CTIS with ID 2023-508524-35-00 check the CTIS register for the current data. The primary objective of this study are 1) to evaluate the safety and determine the highest tolerable dose of NEO-PTC-01 in patients...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON52586

Source
ToetsingOnline

Brief title
NEO-PTC-01 in advanced or metastatic melanoma

Condition

- Other condition
- Metastases
- Skin neoplasms malignant and unspecified

Synonym
Malignant Melanoma, Skin Cancer

Health condition

melanoma

Research involving

Human

Sponsors and support

Primary sponsor: BioNTech US Inc.
Source(s) of monetary or material Support: BioNTech US Inc.

Intervention

Keyword: advance or Metastatic Melanoma, Neoantigens, Personalized T cell, Somatic cell therapy medicinal product (sCTMP)

Outcome measures

Primary outcome

The main study parameter is the assessment of safety of treatment with

NEO-PTC-01 based on incidence of adverse events (AEs), serious adverse

events (SAEs), and changes in safety laboratory values, physical examinations,

and vital signs. Clinical response to treatment will be assessed according to

serial radiographic evaluations (computed tomography [CT] or magnetic resonance

imaging [MRI]) to determine response to treatment and progression of disease

(RECIST v1.1).

Secondary outcome

Clinical response to treatment will be assessed according to serial

radiographic evaluations (computed tomography [CT] or magnetic resonance

imaging [MRI]) to determine response to treatment and progression of disease

(RECIST v1.1). Overall response rate (ORR), defined as the proportion of

patients who achieve a CR or partial response (PR), will be determined.

• PFS, defined as the time from the date of first dosing of NEO-PTC-01 to the

date of first documented progressive disease (PD) or death.

• DOR, defined as the date of the first documentation of a confirmed response

to the date of the first documented PD.

• Clinical benefit rate (CBR), defined as the proportion of patients who

achieve CR, PR, or SD based on RECIST.

• Time to first subsequent therapy, defined as the time from the date of first

dosing to the start date of first subsequent therapy.

Study description

Background summary

NEO-PTC-01 is an autologous personalized T cell product that is manufactured ex vivo and targets neoantigens displayed on the tumor and the tumor microenvironment. Neoantigens are tumor-specific antigens derived of mutations in the DNA presented in the context of the patient*s major histocompatibility complex (MHC) class I and class II alleles. Targeting neoantigens requires an individualized approach and offers an opportunity to tailor the composition of each cell product to generate a personalized T cell product for each patient.

Study objective

This study has been transitioned to CTIS with ID 2023-508524-35-00 check the CTIS register for the current data.

The primary objective of this study are 1) to evaluate the safety and determine the highest tolerable dose of NEO-PTC-01 in patients with unresectable or metastatic melanoma. 2) to evaluate the safety of NEO-PTC-01 in combination with a fixed dose of IL-2 3) to evaluate the safety of NEO-PTC-01 in combination with αPD-1 therapy.

Study design

Study NTC-001 is a Phase 1 investigation of the safety and activity of NEO-PTC-01 in patients with unresectable or metastatic melanoma.
The study will be conducted in two parts, Part 1 (Dose-Finding) and Part 2 (Dose Expansion).
In Part 1, 2 doses are planned; in Part 2, a dose of >= 5.0 x 108 to <= 1.0 x 1010 cells will be used to treat patients.
After the highest tolerated NEO-PTC-01 dose is identified, 2 additional evaluations in Part 1 are planned. A cohort of initially up to 6 patients (with an option to subsequently backfill the cohort with up to 20 patients) is added

to investigate NEO-PTC-01 in combination with IL-2. The IL-2 combination cohort will only be open in countries where IL-2 is approved. Additionally, αPD-1 therapy will be introduced in a separate cohort, beginning 1 to 2 weeks post NEO-PTC-01, to initially up to 6 Part 1 patients who failed αPD-1/αPD-L1 therapy prior to enrollment in NTC-001 (with an option to subsequently backfill the cohort with up to 20 patients).

Intervention

Patients in study Part 1 will receive NEO-PTC-01 beginning at a dose of >= 1x10^8 to <= 1x10^9 cells. Patients in study Part 2 (expansion cohort) will receive NEO-PTC-01 at the highest tolerable dose from Part 1. In Part 2 of the study, patients will continue treatment with PD-1/PD-L1 if the patient initiated such treatment prior to study enrollment. Dose and scheduling are according to SmPCs for the individual products. PD-1/PD-L1 treatment will be stopped a minimum of 2 weeks prior to infusion of NEO-PTC-01. PD-1/PD-L1 treatment is permitted to resume no sooner than 6 weeks after infusion with NEO-PTC-01.

Study burden and risks

NTC-001 is a dose finding and safety First-in-Human (FIH) study of NEO-PTC-01 in patients with unresectable or metastatic melanoma. The dose-finding part of the study is structured according to a 3+3 dose escalation design, limiting exposure to study drug in the initial phase of safety evaluation. As an additional safety precaution, within dose cohorts, enrolment of the first 3 patients will be staggered at a minimum of 2-week intervals.

Major areas of risk include infection during period of lymphodepletion, potential for cytokine release syndrome (CRS), and off-tumor, off-target toxicities. Additional potential risks are those associated with other study-specific procedures, of including tumor biopsies and leukaphereses.

Patients will be hospitalized for inpatient monitoring during the initial treatment phase of lymphodepletion, T cell product infusion, and neutrophil recovery. Thereafter, weekly clinical exam and laboratory monitoring will occur in the outpatient setting from weeks 1-4 post discharge, followed by visits every 6 weeks for the remainder of study.

Safety interventions will include filgrastim growth factor support following the cyclophosphamide + fludarabine lymphodepletion regimen, and cytokine release syndrome (CRS) monitoring and management.

Previous studies with tumor infiltrating lymphocyte (TIL)-based therapies may be the most relevant comparative therapies. These studies are considered in devising a starting dose and dose range for this study. The lower starting dose

is implemented as a core safety consideration for initial NEO-PTC-01 testing in patients.

Assessments from tumor biopsies are critical to the rationale and design of this study. Wherever feasible, the study design allows for use of archival samples for the baseline tumor specimen. Post-infusion tumor biopsy and leukapheresis samples are required to evaluate safety and pharmacodynamic effects, including correlations with toxicity and efficacy in this first-in-human study. These procedures will be performed according to protocol or institutional standards in a hospital-monitored setting.

These risks are considered relative to potential NEO-PTC-01 clinical benefit in patients with unresectable or metastatic melanoma and disease progression or suboptimal response (Part 2) to prior therapies. NEO-PTC-01 represents a novel, individualized treatment approach; addition of neoantigen-specific autologous T cell therapy may offer significant clinical benefit over checkpoint inhibitor regimens.

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

In order to be eligible to participate in this study, a patient must meet all of the following criteria:
1. Adult (age 18 to 75) men and women willing and able to give written informed consent.
2. Histologically confirmed unresectable or metastatic melanoma.
3. Part 1:
a. Have previously received a PD-1/PD-L1 inhibitor (either as single agent or in combination) and a CTLA-4 inhibitor-containing regimen (single agent or combination) prior to NEO-PTC-01, with disease progression following these therapies or otherwise lack of clinical benefit as determined by the study investigator.

Note: Patients who have received a PD-1/PD-L1 inhibitor and ipilimumab (CTLA-4 inhibitor) are eligible. Patients who have discontinued a PD-1/PD-L1 or a CTLA-4 inhibitor due to toxicity and those who are deemed not appropriate to receive a CTLA-4 inhibitor are eligible (except for Part 1 cohort patients to receive additional αPD-1 therapy).
4. Part 2:
a. Have received/are currently receiving a PD-1/PD-L1 inhibitor (as a single agent or in combination with CTLA-4) for at least 3 months.
b. Have documented SD by RECIST 1.1 or clinically asymptomatic progressive disease on the most recent imaging assessment, which must have occurred within 3 months of enrollment.
c. In the opinion of the investigator, are medically eligible and able to continue with PD-1/PD-L1 inhibitor therapy.
d. In the opinion of the investigator, would benefit from the addition of a T-cell-based therapy.
5. For known BRAF mutant patients: Patients must have also received targeted therapy (B-raf inhibitor or B-raf/MEK combination therapy) prior to NEO-PTC-01, unless deemed not appropriate to receive these treatments by the investigator.
6. Have at least 1 site of measurable disease by RECIST 1.1.
7. At least 1 site of disease must be accessible to biopsy for tumor tissue for sequence and immunological analysis. The biopsy site may be the same as the measurable site so long as it remains measurable. Surgical resection of the measurable site may not be performed if that site is the only measurable lesion. An archival biopsy may be used in place if the biopsy was taken within 6 months of informed consent.

8. Have ECOG PS of 0 or 1.
9. Recovered from all toxicities associated with prior treatment to acceptable baseline status (for laboratory toxicities see below limits for inclusion) or an NCI CTCAE version 5.0, Grade of 0 or 1, except for toxicities not considered by the treating physician to be a safety risk (eg, alopecia).
10. Screening laboratory values must meet the following criteria and should be obtained prior to any production phase assessments:
a. White blood cell (WBC) count >= 3 × 103/µL.
b. Absolute neutrophil count (ANC) >= 1.5 × 103/µL.
c. Platelet count >= 100 × 103/µL.
d. Hemoglobin > 9 g/dL or 6 mmol/L.
e. Serum creatinine <= 1.5 × upper limit of normal (ULN) or creatinine clearance >= 50 mL/min by Cockcroft-Gault.
f. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) <= 3 × ULN.
g. Total bilirubin <= 1.5 × ULN (except in patients with Gilbert Syndrome, who can have total bilirubin < 3.0 mg/dL).
h. International normalized ratio (INR), prothrombin time (PT), or activated partial thromboplastin time (aPTT) <= 1.5 × ULN unless the patient is receiving anticoagulant therapy, as long as PT or aPTT is within therapeutic range of intended use of anticoagulants.

Exclusion criteria

A potential patient who meets any of the following criteria will be excluded from participation in this study:
1. Age greater than 75 years or less than 18 years.
2. Received more than 3 prior lines of therapy for metastatic disease.
3. Have an active or history of autoimmune disease (known or suspected). Exceptions are permitted for vitiligo, type I diabetes mellitus, residual hypothyroidism due to autoimmune condition requiring only hormone replacement, psoriasis not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger.
4. Have known active central nervous system metastases and/or carcinomatous meningitis. Patients with previously treated brain metastases may participate provided they are stable (without evidence of progression by imaging [using the identical imaging modality for each assessment, either MRI or CT scan] for at least 4 weeks prior to enrollment and any neurologic symptoms have returned to baseline), have no evidence of new or enlarging brain metastases, and are not using steroids for at least 7 days prior to enrollment. This exception does not include carcinomatous meningitis, which is excluded regardless of clinical and/or radiographic stability.
5. Active systemic infections requiring IV antimicrobial therapy, coagulation disorders or other active major medical illnesses of the cardiovascular, respiratory, or immune system, as evidenced by a positive stress thallium or

comparable test, myocardial infarction, clinically significant cardiac arrhythmias such as uncontrolled atrial fibrillation, ventricular tachycardia, or second- or third-degree heart block, and obstructive or restrictive pulmonary disease.
6. Active major medical illnesses of the immune system including conditions requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalents) or other immunosuppressive medications within 14 days prior to NEO PTC 01 infusion. Inhaled or topical steroids and adrenal replacement doses (<= 10 mg daily prednisone equivalents) are permitted in the absence of active autoimmune disease.
7. Known HIV infection, active chronic hepatitis B or C, and/or life-threatening illnesses unrelated to cancer that could, in the investigator*s opinion, interfere with participation in this study.
8. Have any underlying medical condition, psychiatric condition, or social situation that, in the investigator*s opinion, would interfere with participation in the study.
9. Have a planned major surgery that is expected to interfere with study participation or confound the ability to analyze study data.
10. Are pregnant or breastfeeding, or expecting to conceive or father children within the projected duration of the study, starting with the Screening visit through 120 days after the EOT visit. Nursing women are excluded from this study because there is an unknown but potential risk of AEs in nursing infants secondary to treatment of the mother with treatments to be administered in this study.
11. Have a history of another invasive malignancy aside from melanoma, except for the following circumstances:
a. Patient has been disease-free for at least 2 years and is deemed by the investigator to be at low risk for recurrence of that malignancy.
Patient was not treated with systemic chemotherapy for carcinoma in situ of the breast, oral cavity, or cervix, basal cell, or squamous cell carcinoma of the skin.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-12-2020
Enrollment:	32
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cells autologous

Ethics review

Approved WMO Date:	06-01-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-04-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-06-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-08-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-10-2020
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-10-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-02-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-03-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-06-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-07-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-10-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-11-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO	

Date:	15-12-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-04-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-04-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-04-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-06-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-07-2023
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	CTIS2023-508524-35-00
EudraCT	EUCTR2019-003908-13-NL
CCMO	NL72301.000.19