Development of a GMP protocol for personalized adoptive T-cell therapy

Published: 03-08-2016
Last updated: 15-04-2024

The primary objective is to develop a cell therapy production protocol in line with Good Manufacturing Practice (GMP) regulations by which an autologous T-cell product is generated towards tumor-specific neoantigens. The secondary objective is to…

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON47022

Source
ToetsingOnline

Brief title
Personalized adoptive T-cell therapy protocol

Condition

- Other condition
- Miscellaneous and site unspecified neoplasms benign

Synonym
bladder cancer, head & neck cancer, Lung cancer, melanoma, ovarian cancer

Health condition

Immuuntherapie ontwikkeling

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Vergoeding door het bedrijf NEON Therapeutics

Intervention

Keyword: Immunotherapy, neoantigens, T-cells, therapy protocol development

Outcome measures

Primary outcome

The main study parameter/endpoint per patient will be the number and frequency of T-cell responses that can be generated against tumor neoantigens predicted from the autologous tumor mutanome of the patient.

Secondary outcome

The secondary study parameter/endpoint will be the frequency, phenotype, and functionality of the induced T-cells as characterized by functional assays and flow cytometry.

Study description

Background summary

Recent results have shown that immune-recognition of neoantigens (antigens derived from mutated tumor proteins) plays a large role in the anti-tumor T-cell response. Evidence for this has been demonstrated in immune checkpoint blockade therapy (e.g. anti-PD1, anti-PDL1, anti-CTLA4) and adoptive T-cell therapy where deep and durable clinical responses have been demonstrated. In the majority of cases, neoantigens are unique to each individual*s tumor, necessitating that therapeutic strategies to target them must be individualized. Furthermore, neoantigens are unique therapeutic targets in that their expression is limited only to the tumor and not to *normal* tissue. These targets can be leveraged in the development of new immunotherapies, including personalized adoptive T-cell therapy. In the approach proposed in this study, autologous T-cells are activated and expanded ex vivo against a panel of

neoantigens specific to the individual patient*s tumor. These neoantigen-reactive T-cells are then expanded to large numbers and transferred back into the patient as an adoptive cell therapy. The current study aims to develop a protocol by which this can be achieved, in preparation for a clinical trial testing the safety and efficacy of the treatment.

Study objective

The primary objective is to develop a cell therapy production protocol in line with Good Manufacturing Practice (GMP) regulations by which an autologous T-cell product is generated towards tumor-specific neoantigens. The secondary objective is to characterize and optimize the frequency, phenotype, and functionality of the expanded tumor-reactive T-cells.

Study design

This is a non-therapeutic intervention study that uses patient material to optimize a protocol for personalized adoptive T-cell therapy. The protocol will entail using autologous antigen-presenting cells (e.g. monocyte-derived dendritic cells) that will present tumor-specific neoantigens to stimulate the lymphocytes. All cells used in the protocol will be isolated from the apheresis product or a 200 ml blood sample of a patient.

Study burden and risks

The blood sample taken at the screening phase of the study and the 10 ml blood sample that will be taken at the start of the study will be combined with a treatment-related blood draw whenever possible and should therefore not lead to an extra burden for the patient. The 15 liter apheresis procedure is expected to take around 2-3 hours and may cause some discomfort when inserting the required lines. The apheresis procedure is not associated with any safety concerns, but patients may experience some discomfort such as a dry mouth due to a low level of citrate in their blood after the procedure. When a tumor biopsy is taken during a routine investigation or therapeutic/palliative surgery, this will not cause any extra burden to the patient as these procedures were already planned as part of the treatment. When a tumor biopsy is taken solely for the purpose of this study, this is expected to take around 30 min of the patient*s time. Patients may experience discomfort due to the biopsy (i.e. bruising or pain) and there is a small chance of complications (i.e. infection and/or bleeding). Therefore, biopsies will be taken only from sites that are safely accessible. Standard procedures will be followed in case complications occur, to assure the safety of the patient.

Protocol development is done using healthy donor material as much as possible. However, this study can only be performed in the described study population as the protocol will need to be confirmed to work in patient samples. In addition,

the results obtained with patient material will be required as part of the clinical trial application to demonstrate feasibility and safety of the procedure.

Contacts

Public
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
Amsterdam 1066CX
NL
Scientific
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
Amsterdam 1066CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

a. Age >=18 years
b. Written informed consent
c. Histologically proven NSCLC, bladder, ovarian, melanoma, or head & neck cancer
d. Performance score WHO 0 or 1 at time of study entry
e. An indication for a routine diagnostic investigation or for therapeutic or palliative surgery during which a tumor biopsy can be taken or the presence of metastatic lesion(s) of which a biopsy can safely be obtained

I. Patients with safely accessible metastases according to an interventional-radiologist*
II. Patients not known to have bleeding disorders (such as hemophilia) or bleeding complications from biopsies, dental procedures or surgeries*
f. Expected biopsy size of at least 5 core biopsies or 100 mm3 ;*These criteria are only applicable if the patient will have a biopsy solely for the purpose of this study.

Exclusion criteria

a. Anemia (Hb <6.0 mmol/L)
b. Systemic treatment with steroids (>10 mg) or any other form of immunosuppressive drugs <6 weeks (e.g. prednisone, prednisolone, dexamethasone) prior to apheresis
c. Chemotherapy or radiotherapy <6 weeks prior to apheresis or tumor biopsy
d. History of local therapy administered to the site of tumor biopsy
e. Any active systemic infections or coagulation disorders
f. Presence of a contra-indication for apheresis (platelet count <=100 x 109/L; absolute neutrophil count <=1.5 x 109/L)
g. Positive serology for HIV, hepatitis B, hepatitis C, or lues

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2016
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO

Date:	03-08-2016
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	03-08-2016
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	04-01-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	24-05-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-05-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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
CCMO	NL57848.031.16