Translational research for immune modulating and targeted therapy in advanced or metastatic non-small cell lung cancer, an exploratory NVALT study

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON23268

Source
Nationaal Trial Register

Brief title
Translational research for immune modulating and targeted therapy in advanced or metastatic NSCLC

Health condition

Non-small cell lung cancer
Niet-kleincellig longkanker

Sponsors and support

Primary sponsor: NVALT
Source(s) of monetary or material Support: NVALT

Intervention

Outcome measures

Primary outcome

• Relation between adaptive and innate immune status and tumor response rate, PFS and OS.

• Relation between gate keeper mutations and complex mutations with tumor response rate, PFS and OS on treatments used by treating physician.

• Correlation of the baseline ctDNA level with tumor response rate, PFS and OS

• Correlation of the change in ctDNA level after six weeks of treatment to ORR, PFS and OS.

• Validated tumor educated platelet algorithm that is associated with increased ORR, PFS and OS.

• Validated tumor educated platelet algorithm that is associated with therapy resistance.

• Correlation of STM-panel based response assessment with radiological response assessment as performed by CT-thorax.

• Correlation of PBMC FACS parameters of lymphoid and myeloid subsets in peripheral blood to tumor response rate, PFS and OS.

• Correlation of rare mutation profile, as assessed by NGS on tumor tissue, to tumor response rate, PFS and OS.

• Correlation of tumor tissue IHC parameters to tumor response rate, PFS and OS.

• Correlation of RNAseq on fresh frozen tumor tissue to tumor response rate, PFS and OS.

• Correlation of CT based parameters to tissue parameters and tumor response rate, PFS and OS.

• Correlation of differences between CT based (textural) parameters and tissue parameters and tumor response rate.

Secondary outcome

-

Study description

Background summary

In this study we will explore frozen and paraffin embedded (FFPE) tumor tissue and blood samples from patients that are eligible for immune- and targeted therapy and those who

become resistant to immune- and targeted therapy after an initial response. Frozen tumor biopsies will be used for RNA seq and FFPE tissue will be stained with multiple fluorescent targets to identify stimulating and inhibiting immune cells in the tumor. Moreover, blood will be collected to explore the role of circulating blood markers.

Study objective

1. The predictive biomarkers for tumor response to immuno modulating therapy will be a combination of adaptive and innate immune status per patient that will be estimated with a tumor biopsy before, 6 weeks after start treatment (optional) and at progression or recurrence of disease and blood sampling at baseline, in week 2 or 3, 6, 12 and at progression or recurrence of disease. This status can be defined as the different immune cell fractions estimated by CIBERSORT and the LM22 leukocyte signature matrix estimated from RNA sequencing data. Another approach is looking for activating T8+ cells and inhibitory Treg, macrophages and myeloid suppressor cells by immune fluorescence tests in the same biopsy by multispectral imaging. In combination with clinical data the meaning of the different fractions can be assessed in a prospective way.

2. Resistance to targeted therapy that develop early in the course of disease will be limited to gate keeper mutations and a complex delayed resistance due to a multitude of mechanisms.These resistance mechanisms can be discerned by a biopsy from the growing tumor. DNA and RNA seq data will used to illuminate patterns of resistance.

Study design

Blood sampling: 1 whole blood and 2 EDTA at baseline, week 2 or 3, week 6, week 12 and at progression or recurrence of disease.

Tumor biopsie will be taken at baseline, week 6 and at progression or recurrence of disease.

Intervention

Blood drops and optionally a tumor biopsy

Contacts

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Eligibility criteria

Inclusion criteria

1. Eligible for immunotherapy or targeted treatment.

2. Written informed consent for registry of patient data and extra blood and tumor biopsy.

3. Age 18 years and older.

Exclusion criteria

1. Without written informed consent patient will be adopted anonymously in the registry and will not take part of the study.

2. Patients with written informed consent for registry of patient data but no consent for extra blood and tumor biopsy will be excluded from the study.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2017
Enrollment:	300
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL6218
NTR-old	NTR6390
Other	2017/217 : METC

Study results