Implementation of up-front ctDNA analysis into lung cancer care and development of liquid biopsy-based decision support models - the Lungmarker2 study

Published: 15-06-2023
Last updated: 25-03-2025

This study implements up-front ctDNA analysis ('plasma first approach') into routine diagnostic work-up of all advanced stage LC patients in the Southeast of the Netherlands (the participating hospitals in the OncoZON region). Thereby,...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory tract neoplasms
Study type	Observational invasive

Summary

ID

NL-OMON53764

Source
ToetsingOnline

Brief title
LM2 study

Condition

- Respiratory tract neoplasms

Synonym
lung cancer, lung carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Catharina-ziekenhuis
Source(s) of monetary or material Support: Eigen onderzoeksgeld en een bijdrage van een bedrijf,Roche Diagnostics Nederland B.V.

Intervention

Keyword: decision support models, liquid biopsy, lung cancer

Outcome measures

Primary outcome

ctDNA analysis, as additional source of genetic information, is integrated into the diagnostic workup of LC patients and the medical benefits thereof are quantified, i.e. a significant higher percentage of patients with a driver mutation are identified by the plasma first approach. Multiparametric decision support algorithms based on imaging, TM and ctDNA analyses that identify small-cell LC (SCLC) and non-small-cell LC (NSCLC) are developed and validated. Multiparametric decision support models are developed that enable patient-specific timing of imaging procedures during follow-up of LC patients. A super-resolution microscopy test for PD-L1 is developed and correlation with tumor tissue PD-L1 expression has been established.

Secondary outcome

An analytical protocol for analysis of PD-L1 expression on CTCs by super-resolution microscopy has been developed.
All LC patients with a molecular aberration and all SCLC patients have been followed up by liquid biopsy during treatment.
The number of NGS analyses and time to diagnosis decreased by introduction of

up-front LB.

Study description

Background summary

In the Netherlands, 14,700 new patients were diagnosed with lung cancer (LC) in 2021. LC ranks sixth regarding burden of disease, and first compared to other malignancies. Diagnosis is based on imaging and histopathology/cytology of suspicious tissue. Depending on tumor type and stage, additional analyses like next-generation sequencing (NGS) and protein analysis on tissue are needed. With new, biomarker-based therapeutic options that improve survival, it is of importance to obtain all relevant tumor characteristics to ensure the best match between tumor and therapy. Tumor biopsies are not always informative, and many patients undergo re-biopsies, increasing patient burden and strain on health care resources. Still, for a substantial number of patients, information required for decision making is lacking and a significant number of patients with poor performance status die before therapy is started.
Liquid biopsy (LB) is the analysis of tumor remnants, e.g. circulating tumor cells (CTCs), circulating tumor DNA (ctDNA) and tumor-enhanced endogenous proteins (tumor markers, TMs), in body fluids and can be used as complementary source of tumor information. Despite scientific evidence, use of LB in diagnosis and monitoring of lung cancer (LC) is limited since it requires major changes in diagnostic and care pathways. Analyzing TMs, CTCs and ctDNA in blood can inform about the nature of the tumor, the most appropriate therapy, therapy response and resistance.

Study objective

This study implements up-front ctDNA analysis ('plasma first approach') into routine diagnostic work-up of all advanced stage LC patients in the Southeast of the Netherlands (the participating hospitals in the OncoZON region). Thereby, additional information about the molecular make-up of the tumor becomes available, the number of tissue NGS analyses will decrease and time to therapeutic decision making is shortened. Next, using ctDNA, TM and other information, multiparametric decision support models are built and validated that may support diagnosis, predict the outcome of the next imaging procedure and progression-free survival during follow up. The final goal is to develop a super-resolution microscopy test that can detect PD-L1 expression on CTCs.

Study design

Multicenter, prospective, implementation and diagnostic cohort study

Study burden and risks

At diagnosis, an extra 10 mL of blood are drawn during a routine venipuncture. If the subject has advanced stage LC, an additional venipuncture is performed and 40 mL of blood are drawn for ctDNA analysis. Some of the patients undergo LBs during treatment. The follow up period is 36 months max. with a maximum of 20 blood draws. The volume per draw ranges from 10-40 mL. The risks of a venipuncture are negligible and the burden minimal.

Contacts

Public
Catharina-ziekenhuis

Michelangeloolaan 2
Eindhoven 5623EJ
NL
Scientific
Catharina-ziekenhuis

Michelangeloolaan 2
Eindhoven 5623EJ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

first work-up for suspected lung cancer

Exclusion criteria

Presence of another malignant tumor, i.e. diagnosed with a tumor in the past 5 years

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	31-10-2023
Enrollment:	800
Type:	Actual

Ethics review

Approved WMO Date:	15-06-2023
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-09-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-11-2023

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-02-2025
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL83276.100.22