Lung cancer Early Molecular Assessment trial

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Primary Objective:- To determine the percentage of patients with EGFR mutation, ALK translocation and other genetic aberrations with an improved efficacy of molecular profiling in all stages of NSCLC.- To determine PD-L1 tumour proportion score in...

Ethical review	Approved WMO
Status	Pending
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON47319

Source
ToetsingOnline

Brief title
Lung cancer Early Molecular Assessment trial:LEMA

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
non-small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Astra Zeneca,Farmaceutische Industrie: AstraZeneca;Merck Sharp & Dohme (MSD);Roche Pharma and Diagnostics,Merck Sharp & Dohme (MSD),Roche Pharma and Roche Diagnostics

Intervention

Keyword: Early molecular assessment, liquid biopsies, NSCLC, tissue biopsies

Outcome measures

Primary outcome

The percentage of patients with EGFR mutation or ALK translocation using the combined tumour tissue and liquid biopsy analysis.

Secondary outcome

Secondary endpoints include the test performance of both techniques in different stage of disease, the percentage of patients with a predefined actionable genetic alteration, the costs, and the influence of the liquid biopsies on the diagnostic yield of tissue molecular and pathological analysis.

Study description

Background summary

Non-small lung carcinoma (NSCLC) has a poor prognosis. At presentation 50-60% of patients have stage I-III disease for which curative therapy is available. But, in the majority of these patients the disease will metastasize and systemic treatment is needed during the course of the disease. For metastasized disease the 5-year overall survival rate is less than 5%.
Personalized treatment has become standard of care for metastasized NSCLC but the proportion of patients for which targeted agents are available is still modest. Next to targeted therapy currently immunotherapy is being introduced. Targeted therapy is available for patients with EGFR and ALK gene aberrations and many other targets are to be expected in the oncoming few years. For patients with NSCLC wild-type ALK and EGFR, only chemotherapy is for first line treatment that is often less effective than targeted therapy and has an inferior toxicity profile. For patients that present with earlier stage disease (stage I-III) currently no targeted agents have been approved. As of now, when patients present with disseminated disease, molecular profiling is initiated.
The process of retrieving biopsy material from another hospital or collecting a new biopsy, together with the molecular analysis itself can easily take up to 5 weeks. For approximately a quarter of patients, these samples are not available

in sufficient amount to perform predictive mutation analysis. Therefore a substantial number of patients receives no targeted treatment. When however, molecular profiles are available at an earlier stage of disease, more patients who develop disseminated disease might benefit from personalized therapy opportunities. Also because there is more time available we can perform the molecular profiling in a cost-effective manner (that is sequentially and not parallel), which will reduce the diagnostic costs. Although this strategy resolves the delay to obtain a molecular diagnosis in the metastasized setting, it won*t resolve the problem of insufficient material obtained with biopsy. Therefore, we will use both tissue and blood-based genetic testing. We hypothesize that early molecular screening will enable a timely switching to targeted treatment and significantly improve survival and diagnostic efficiency.

Study objective

Primary Objective:
- To determine the percentage of patients with EGFR mutation, ALK translocation and other genetic aberrations with an improved efficacy of molecular profiling in all stages of NSCLC.
- To determine PD-L1 tumour proportion score in all stages of NSCLC

Secondary Objective(s):
- To define the diagnostic value of liquid- and tissue biopsy-based molecular analysis.
- To investigate the change in diagnostic yield of tissue-based molecular analysis when blood-based molecular analysis is an available alternative.
- To explore the reasons for insufficient tumor material available for molecular profiling.
- To define the frequency of pre-defined genetic alterations using the LEMA approach.
- To estimate the costs of the LEMA approach and the introduction of liquid-based analysis
- To compare results of molecular analysis at baseline and follow up of NSCLC.
- To explore the epidemiology of the PD-L1 biomarker expression in all stages of NSCLC.
- To determine PD-L1 tumour proportion score in EGFR mutant and ALK rearranged NSCLC

Study design

In this prospective multicentre trial tumours of all patients presenting with NSCLC will be profiled upfront, irrespective of disease stage and pathology using both tissue and blood-based genetic testing. A minimal molecular profiling is depicted but other targets will be included in due time. The study is divided in two parts. In the first part participating centres will have a

run-in period of half a year in which molecular profiling is performed as is currently standard of care. This period will be used to measure the impact of increased awareness on the diagnostic process. During the second part of the study a comprehensive upfront profiling according to local standards will take place for all NSCLC patients. Liquid (blood) biopsies will be included in order to increase the diagnostic yield for those patients where tissue biopsies are not adequate. Patients will be treated according to standard of care, or included in clinical studies where appropriate. Re-biopsies (both tissue and liquid) will be advocated at the time of establishing disease progression/disseminated disease, and personalized therapy will be initiated according to the existing data from the molecular profiling.

Study burden and risks

The expected diagnostic process will change and theoretically the number of biopsy procedure might be increased and therefore the chance of minor complications. However, the improved molecular profiling is thought to expand treatment opportunities. Patients will benefit from a direct switch to targeted treatment upon progression.

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

- Suspicion of lung carcinoma or established NSCLC but awaiting start of definitive treatment
- Written informed consent to undergo diagnostic procedure and molecular analysis of the disease.

Exclusion criteria

- Not motivated to receive any treatment at any point in time. Patients who consider undergoing treatment in the future are eligible.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2016
Enrollment:	1297
Type:	Anticipated

Ethics review

Approved WMO Date:	31-05-2016
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	13-10-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-01-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-03-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-08-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-04-2018
Application type:	Amendment
Review commission:	METC NedMec

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	NL54778.031.15