Identification of the immune response against tumour antigens in patients with lung adenocarcinoma

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

Summary

ID

NL-OMON56899

Source
ToetsingOnline

Brief title
XAGE

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
adenocarcinoma, lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: adenocarcinoma, immune response, lung, XAGE

Outcome measures

Primary outcome

The primary objective of this study is

- to assess the presence, type and strength of XAGE-1B-specific cellular immune responses of lung cancer patients in the peripheral blood, mediastinal lymph nodes and the primary tumour.

- to assess the expression of the XAGE-1B antigen in the primary lung tumor

Secondary outcome

- the presence, type and strength of XAGE-1B-specific cellular immune response in the primary tumour of patients that undergo tumour resection after diagnostic work-up

- the presence, type and strength of antigen-specific cellular immune responses against potential other tumour antigens (including p53 and HPV16) in lung adenocarcinoma patients

- whether the presence of a specific cellular immune response is associated with a certain type of lung adenocarcinoma patients.

- whether chemotherapy enhances the activation of systemically present antigen-specific immune response.

- whether there exists a relation between the presence of a specific immune response and clinical outcome of patients with lung adenocarcinoma

Study description

Background summary

Lung cancer is the most common cause of cancer mortality in men in the developed world and one of the leading causes in women. In the Netherlands, around 9000 new cases of lung cancer occur annually. The male-female ratio in the occurrence of lung cancer is 80%-20%. Each year around 9000 patients die from lung cancer in the Netherlands. The two major forms of lung cancer are non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLC comprises about 80 % of all lung cancers. Smoking is the main (environmental) risk factor that is associated with the development of lung cancer.
Establishing the mechanisms involved in the development of lung cancer has been the subject of intensive investigation in recent years.

Determining the stage of disease is critical for treatment recommendations and prognosis. Lung cancer patients are staged according to the TNM classification system. Patients with stage I and stage II non small cell lung cancer are, when operable, treated with complete surgical resection. Patients with advanced disease (stage III/IV) are generally treated with chemotherapy, radiotherapy or a combination of both. This treatment is palliative, mostly has a partial respons and quick progression of disease occurs regularly. Unfortunately, the majority of lung cancer patients present with advanced disease. Therefore, the five-year survival for non small cell lung cancer patients is low (14%)

Recent research has therefore focused on new anticancer therapies regarding lung cancer. Recently, immunotherapy has been shown to have great potential as a new anticancer therapy in several malignancies (melanoma, vulva carcinoma). Whether immunotherapy can be used in the treatment of lung cancer, depends on whether a specific immune response can be found in these patients and on which tumorantigens are involved. XAGE-1B is a member of the family of cancer testis (CT) antigens and appears to evoke an immune response in patients with lungadenocarcinoma. So far, XAGE-1B specific systemic or local cellular immune responses have not been studied in patients with lung adenocarcinoma or other types of NCSLC.

Study objective

This is an exploratory study to assess the presence, specificity, type and strength of systemic and local specific cellular immune responses in patients with lung adenocarcinoma at different time-points during routine diagnostic work-up and treatment. This study will be performed in order to delineate the immunological setting in which potential vaccines could be used as treatment options for lung cancer patients.

Study design

All patients presented at the Department of Pulmonology with lung adenocarcinomas, undergoing routine diagnostic work-up and treatment will be asked to participate in our study. So far, XAGE-1B expression has only been reported in lung adenocarcinomas. It has been observed that around 30% of lung adenocarcinomas are positive for XAGE-1B (Nakagawa CCR 2005; our own non-published observations). For the primary study objective we aim to include at least 15 patients with XAGE-1B expressing tumours. Therefore, we plan to recruit at least 60 patients with adenocarcinomas in order to investigate the presence of a XAGE-1B specific systemic or local immune responses.. Following informed consent the following materials will be collected:

For the analysis of systemic and local specific T-cells and for the analysis of tumour-antigen expression and immune-infiltrate

- From all patients, we will collect heparin blood samples (70 ml) taken at a maximum of 2 weeks before treatment. From those patients that will undergo chemotherapy (stage II/IV lung adenocarcinoma patients), we will also collect 70 ml of blood 2-4 weeks after the last dose of the chemotherapy schedule. The heparinized blood samples will be collected via venapunction at outpatient clinical visit. This blood will be collected together with the routine regular venapunctions.

- From those patients who will undergo mediastinal staging by endoscopic ultrasound guided fine needle aspiration (FNA), we will collect mediastinal lymph node aspirates.

- From those patients that undergo bronchoscopy or CT-guided biopsy during diagnostic work-up, fresh biopsy material will be obtained.

- From those patients that undergo lung surgery after diagnostic work-up, fresh tumour resection tissue will be obtained.

Study burden and risks

The collection of all materials will be performed during the standard outpatient visits and clinical admissions as part of routine diagnostic procedures and treatment of lung cancer patients. In addition to this, we will ask patients for an additional 70 ml of blood prior to treatment. After treatment with chemotherapy, we will also ask for an additional 70 ml of blood. We will collect these blood samples by venapunction during routine outpatient clinical visits. Furthermore, we will ask lung cancer patients who are staged by endoscopic ultrasound guided fine needle aspiration, for permission to perform 2 additional lymph node punctions next to the regular 4 punctions that are routinely performed during these procedures. These two extra nodal

aspirates will prolong the procedure, which normally takes 15-20 minutes, with an estimated 4 minutes and does not pose an increased risk for the patient.

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

Patients with suspected or proven lung adenocarcinoma who will undergo endosonograpgy in order to pre-operatively stage the mediastinum for lymph node metastases.

Exclusion criteria

No adenocarcinoma

No clinical indication for undergoing endosonography

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-04-2011
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	01-02-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL32145.058.10