CA209-762: Pilot study of fine needle aspiration (EUS/EBUS) versus histology for PD-L1 staining in lung cancer, a pilot study.

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

Summary

ID

NL-OMON45681

Source
ToetsingOnline

Brief title
FNA vs histology for PD-L1 staining in lung cancer

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Non-small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Bristol-Myers Squibb,grant

Intervention

Keyword: FNA versus histology, Nivolumab, NSCLC

Outcome measures

Primary outcome

Explore the agreement between cytology blocks and routine histology tissue, both stained for the presence of PD-L1.

Secondary outcome

Explore for which patients with PD-L1 expression, the treatment with PD-1/PD-L1 inhibitors will lead to a durable response. A durable response is defined by having clinical benefit from a PD-(L)1 inhibitor for at least one year of treatment. For that, the included patients being treated with PD-(L)1 inhibitors, will be divided into two groups (those with durable response versus those without durable response).

Study description

Background summary

PD-L1 status is determined on histological specimen only. No data on PD-L1 staining are available for cytology specimen obtained by EUS/EBUS. Lung cancer tumors are often centrally located and diagnosis is most easily obtained by EUS/EBUS cytology. These diagnostic procedures show very little complications as opposed to histological procedures like CT guided core biopsies, peripheral bronchial biopsies or core biopsies from metastatic sides such as the liver. Therefore, we would like to explore whether PD-L1 status from tumor tissue by fine needle aspiration is comparable to a routine histological biopsy in these patients. To evaluate the clinical relevance, we would like to explore which patients with PD-L1 expression as assessed by fine needle aspiration are good responders on the treatment with PD(-L)1 inhibitors.

Study objective

The primary objective for this study is to explore the options for a minimally invasive predictive test for selecting patients for the treatment with an anti-PD1/PD-L1 treatment.
The secondary objective is to explore for which patients with PD-L1 expression, the treatment with PD-1/PD-L1 inhibitors will lead to a durable response. A durable response is defined by having clinical benefit from a PD-(L)1 inhibitor for at least one year of treatment. For this purpose, results of PD-L1 expression as collected by fine needle aspirations via EUS/EBUS/ECHO will be compared to routine histology of the primary tumor and related to a durable response to PD1 inhibition (nivolumab).

Study design

For this explorative study 40 patients with non-small cell lung cancer [both squamous and non-squamous histology] with both a fine needle specimen (22 Gouch, FNA) and a routine histological tumor biopsy before receiving nivolumab 240 mg every 2 weeks. FNA from both primary tumor and lymph node. Immune status of the patients will be monitored at the start and after treatment. Patients will be followed up for at least one year

Study burden and risks

As part of the trial, patients will be expected to attend several clinic visits. This is not different from the standard of care. Patients will undergo physical examinations, vital sign measurements (including oxygen saturation levels), blood tests for safety assessment, pregnancy testing (for females of child bearing potential), and monitoring for adverse events. In addition, every 6 weeks (from week 6 until week 49) and then every 12 weeks, patients will undergo radiographic assessment of their tumours (by PET/CT) until disease progression or clinical benefit. Blood will also be collected at certain visits for research
purposes (biomarker). The frequency of visits and number of procedures carried out during this trial will generally be considered standard of care. These procedures are conducted by medically trained professionals and every effort will be made to minimise any risks or discomfort to the patient. Treatment for cancer often has side effects, including some that are life threatening.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Histologically confirmed stage IIIB and stage IV NSCLC
2. Smokers or ex-smokers with at least 15 Pack Years.
3. The tumor tissue sample must be fresh, preferably fresh frozen, in addition to routine FFPE-tissue processing from the primary tumor, core needle biopsy, excisional or incisional biopsies are accepted. Fine needle biopsies and drainage of pleural effusions with cytospins are not considered adequate as primary tumor biopsy sample.
4. Cytology will be obtained by either esophageal ultrasound (EUS), endobronchial ultrasound (EBUS) or ECHO guided fine needle aspiration of the same lesion that histology was obtained (preferably the primary tumor) and of a lymph node metastasis. Cytology will be obtained by rapid onsite cytology (ROSE), to ascertain sufficient tumour cells as assessed by an experienced laboratory technician.
5. Prior palliative radiotherapy must have been completed at least 2 weeks prior to first dose nivolumab.
6. Any line of previous chemotherapy.
7. At least one unidimensionally measurable lesion according to RECIST1.1 criteria.
8. Life expectancy more than 3 months.
9. ECOG PS 0/1.
10. Age 18 years and older, both male and female subjects.

11. Adequate organ functions.
12. Signed informed consent.

Exclusion criteria

1. Previous treatment with PD-1 or PD-L1 inhibitor.
2. Pregnant or lactating women.
3. Patients who are poor medical risks because of non-malignant disease as well as those with active uncontrolled infection.
4. Patients without plasma sample at baseline (before treatment).
5. Patients are excluded if they have active brain metastases or leptomeningeal metastases. Subjects with brain metastases are eligible if metastases have been treated and there is no magnetic resonance imaging (MRI) evidence of progression for at least 4 weeks after treatment is complete and within 28 days prior to the first dose of nivolumab administration. There must also be no requirement for immunosuppressive doses of systemic corticosteroids (> 10 mg/day prednisone equivalents) for at least 2 weeks prior to study drug administration.
6. Patients receiving palliative radiotherapy to the primary tumor will be excluded.
7. Subjects with carcinomatous meningitis.
8. Subjects must have recovered from the effects of major surgery or significant traumatic injury at least 14 days before randomization.
9. Subjects with previous malignancies (except non-melanoma skin cancers, and the following in situ cancers: bladder, gastric, colon, cervical/dysplasia, melanoma, or breast) are excluded unless a complete remission was achieved at least 2 years prior to study entry and no additional therapy is required or anticipated to be required during the study period.
10. Other active malignancy requiring concurrent intervention.
11. Subjects with an active, known or suspected autoimmune disease. Subjects with type I diabetes mellitus, hypothyroidism only requiring hormone replacement, skin disorders (such as vitiligo, psoriasis, or alopecia) not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger are permitted to enroll.
12. Subjects with a condition requiring systemic treatment with either corticosteroids (>10 mg daily prednisone equivalent) or other immunosuppressive medications within 14 days of randomization. Inhaled or topical steroids, and adrenal replacement steroid doses > 10 mg daily prednisone equivalent, are permitted in the absence of active autoimmune disease.
13. Subjects with interstitial lung disease that is symptomatic or may interfere with the detection or management of suspected drug-related pulmonary toxicity.
14. Known history of testing positive for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome (AIDS).
15. Any positive test for hepatitis B virus or hepatitis C virus indicating acute or chronic infection.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-07-2017
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	09-05-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 25545
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL60183.042.16

Register	ID
OMON	NL-OMON25545