'Comparison of EUS/EBUS-guided fine needle aspiration and PET-CT in the restaging after induction therapy of locally advanced non-small cell lung cancer'.

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1. This study aims to compare the accuracy of EUS/EBUS and PET-CT as restaging tools in patients treated with induction therapy for stage IIIA or IIIB NSCLC.2. To study the additive value of immune histochemical staining of adequate biopsies...

Ethical review	Approved WMO
Status	Pending
Health condition type	Respiratory tract neoplasms
Study type	Interventional

Summary

ID

NL-OMON29867

Source
ToetsingOnline

Brief title
EUS/EBUS-FNA and PET-CT in restaging nsclc.

Condition

- Respiratory tract neoplasms

Synonym
(diagnosis of) non-small-cell-lungcancer, lung cancer.

Research involving
Human

Sponsors and support

Primary sponsor: Isala Klinieken
Source(s) of monetary or material Support: maatschap longziekten.

Intervention

Keyword: EBUS, EUS, PET-CT, restaging nsclc

Outcome measures

Primary outcome

1. Accuracy of PET-CT and E(B)US in restaging NSCLC after induction therapy.

Secondary outcome

1. Accuracy of E(B)US when adding immune histochemical analysis to

tumour

negative but cytologic adequate samples.

Study description

Background summary

Restaging after induction therapy of advanced non small cell lung cancer (NSCLC) has been shown to be very important to determinate prognosis1-4 . The choice of local therapy (surgery or radiotherapy) might be influenced by the persistence of N2 or N3 disease as is studied at the moment by the Dutch NVALT 6 study. Superiority of local therapy in downstaged patients is under investigation. An EORTC proposal with randomization between radiotherapy or surgery after downstaging is prepared at the moment. Restaging procedures to be considered are re-mediastinoscopy, PET-CT, endoscopic ultrasound guided fine needle aspiration (EUS-FNA) and endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA). Results of re-mediastinoscopy were disappointing demonstrated by 40% incomplete procedures due to fibrosis in a study of 15 patients5. PET-CT is by far superior to re-mediastinoscopy 6. Endoscopic ultrasound (EUS) is feasible in mediastinal restaging (7), but covers just a part of the mediasinum. Endobronchial ultrasound (EBUS) is developed more recently and also showed to be very useful in staging the mediastinum (8,9). Restaging studies with EBUS have not been published untill now. Combining both ultrasound modalities showed the complementarity of EUS and EBUS in staging the

mediastinum (10). The accuracy of a combined approach of EUS-FNA and EBUS-TBNA was 100% for the diagnosis of mediastinal cancer in a group of 28 patients (11). On theoretical grounds it seems reasonable to assume that the combination of EUS and EBUS makes an exploration of all mediastinal lymph nodes possible to a greater extend than mediastinoscopy. Superiority of EUS-FNA over mediastinoscopy was demonstrated in a study of 60 patients having both diagnostic investigations for mediastinal staging of NSCLC (12).
Since resolution of ultrasound techniques is high and fine needle aspirations are real-time it is expected that a combination of EUS and EBUS has a higher accuracy than PET-CT and could become the preferred restaging tool in near future. To prove this hypothesis we have to compare both modes of restaging in a prospectively designed study. Therefore all patients with stage III treated by induction therapy(chemotherapy or chemoradiotherapy) will be analysed with PET-CT and EUS/EBUS as restaging tools. False negative findings could be caused by sampling errors or false interpretations by the cytopathologist of specimens with tumour cell poverty. Especially pre-treated nodes with diminished tumour burden could theoretically raise this false negative rate. Although sampling errors will remain a problem, the question rises if the more sensitive immune histochemical analysis could modify EUS-FNA and EBUS-TBNA results. In order to answer this question, biopsies obtained by EUS-FNA and EBUS-TBNA and blocked in Agar-agar to make them suitable for immune histochemical analysis, will retrospectively be analysed for patients with false-negative restaging results proven by thoracotomy and lymph node dissection.

Study objective

1. This study aims to compare the accuracy of EUS/EBUS and PET-CT as restaging tools in patients treated with induction therapy for stage IIIA or IIIB NSCLC.

2. To study the additive value of immune histochemical staining of adequate biopsies without obvious tumour cells at routine microscopy.

Study design

prospective, open, single-arm trial.

Hundred patients with an age between the18-85 years treated with induction therapy (chemotherapy and / or radiotherapy) for stage IIIA or IIIB NSCLC will be recruited at the outpatient clinic of the pulmonology department. All patients will undergo PET-CT and EUS-FNA and / or EBUS-TBNA before and after induction therapy. Both PET-CT scans will be compared and the decline in standard uptake value will be quantified. This decline will be correlated with the results of restaging by means of ultrasound guided aspirates (EUS and EBUS). Verification of negative cytologic results will be done by surgical procedures like mediastinoscopy or preoperative lymph node dissections.

Patients will be (preferably) re-staged with the same procedure as in initial analysis before induction treatment. If the patient was staged initially by mediastinoscopy, the re-staging ultrasound procedure will be determined by the localisation of lymph node metastasis. The approach of right sided paratracheal lymph nodes and pretracheal lymph nodes is generally by EBUS-TBNA whereas the other localisations could be biopsied with EUS-FNA. The subcarinal nodes can be reached by either mode of ultrasound guided biopsy. The next possibilities could occur in the diagnostic approach:

1. PET-CT shows activity in the lymph nodes, but EUS-FNA detects no tumorous cells; mediastinoscopy will follow.

2. PET-CT shows no activity in the lymph nodes and EUS-FNA detects no tumorous cells, surgery (seldom radiotherapy) will be undertaken.

3. PET-CT shows activity in the lymph nodes and EUS-FNA detects tumorous cells, surgery is excluded.

4. PET-CT shows no activity in the lymph nodes, but EUS-FNA detects tumorous cells, surgery is excluded.

Besides routine cytological analysis on stained slides, the specimen obtained with EUS-FNA or EBUS-TBNA will be caught in a diagnostic tube, fixed with carbowax and centrifuged to a cellular cast. This pellet of cells will be fixed in agar-agar, sliced and used for immunehistochemical analysis. The slides will be analysed by an experienced cytopathologist in those cases where standard cytological investigations showed adequate lymphogenic material but no tumour cells and only in patients where the results showed to be false negative after a *golden standard procedure* such as thoracotomy with mediastinal lymph node dissection. The accuracy of EUS/EBUS and PET-CT separately and in combination as restaging tools in stage IIIA or IIIB NSCLC patients after induction therapy will be determinated. The additive value of immune histochemical staining of adequate biopsies without obvious tumour cells at routine microscopy will also be evaluated. Patients who seem to be downstaged (EUS/EBUS and PET-CT negative) will proceed to thoracotomy. Resection of tumor and mediastinal lymph node dissection is obligatory. PET-CT*s of patients who are excluded from surgery, but who are candidates for adjuvant radiotherapy, could be used by the radiotherapist to detect the exact radiotherapy field.

Intervention

All patients will undergo PET-CT and dependent on these findings EUS-FNA

and / or EBUS-TBNA or mediastinoscopy will be performed. Immunehistochemical analysis will be performed retrospectively by a cytopathologist in cases of negative finding after surgical verification.

Study burden and risks

Patients are at risk for infection and bleeding. These investigations are, however, also part of the regular diagnostic work-up and biopsies are inevitable for the definite diagnosis.

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

1. patients treated with induction therapy for stage IIIA or IIIB NSCLC.
2. age of 18-85 years

Exclusion criteria

1. comorbidity (alcoholabuse, drugsabuse and psychiatric disease limiting decision making).
2. non-compliance.
3. previous re-staging after induction therapy.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2006
Enrollment:	100
Type:	Anticipated

Ethics review

Approved WMO

Date:	10-08-2006
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)

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	NL12527.075.06