Evaluation of 3'-deoxy-3'-[18F]fluorothymidine -PET and diffusion weighted imaging -MRI in patients with early stage non-small cell lung cancer treated with a platinum-based doublet as preoperative chemotherapy.

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Primary objectives* 18F-FLT-PET/CT: - To correlate the percentage change in SUV between baseline (SUV-1) and early therapy (SUV-2) with pathological quantification (% of viable tumor cells) of the primary tumor after pre-operative chemotherapy in...

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

Summary

ID

NL-OMON42040

Source
ToetsingOnline

Brief title
Preoperative PET and MR study in lung cancer patients

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Lungcancer, non-small cell lung cancer

Research involving

Human

Sponsors and support

Primary sponsor: European Organisation for Research in Treatment of Cancer (EORTC)
Source(s) of monetary or material Support: IMI-consortium

Intervention

Keyword: DW-MR, FLT-PET, NSCLC, Preoperative chemotherapy

Outcome measures

Primary outcome

* Percentage of ADC change at day 14 (i.e. ADC-2) relative to baseline (i.e.

ADC-1)

* Percentage of FLT uptake change at day 14 (i.e. SUV-2) relative to baseline

(i.e. SUV-1)

* Pathological quantification (% viable tumor cells) measured in surgical

specimens

Secondary outcome

* Pre-operative (post-treatment) ADC measurement (i.e. ADC-3)

* Pre-operative (post-treatment) FLT uptake measurement (i.e. SUV-3)

* Tumor volume (baseline and pre-operative) measured by CT or MRI

* Immunohistochemistry (IHC) of cell proliferation marker Ki-67-index in

diagnostic biopsy samples (if available) and surgical specimens.

* Metabolic change in FDG-PET (baseline and pre-operative, if available)

* Safety

Study description

Background summary

Response assessment in NSCLC is usually performed according to CT scans of the thorax. Vigorous debate has challenged the use of anatomic assessments alone such as conventional CT and MRI, as it may take two or three months to detect any tumor shrinkage. In addition, it has been observed that changes in tumor metabolism are more significant than anatomical changes in lung cancer patients. Thus only morphological information may not be a suitable tool to assess early treatment response. Furthermore with the development of targeted chemotherapy agents, which are primarily cytostatic, methods of assessing the biological response of a tumor becomes increasingly relevant, because reduction in tumor size will not always be expected and conventional imaging will not suffice.

Therefore, there is an unmet need for methods assessing therapeutic effectiveness by criteria other than morphological measurements. In this regard, early tumor response assessment imaging biomarkers that quantify cell proliferation by 18[F]-fluorothymidine (18F-FLT) using PET and cell death by apparent diffusion coefficient (ADC) using diffusion weighted magnetic resonance imaging (DWI-MRI), could together provide a more detailed insight into a tumor*s microenvironment. In previous studies it was proven that the percentage of viable tumor cells in pathological evaluation is a significant predictor of OS and disease free survival (DFS) in NSCLC patients treated with preoperative chemotherapy. In this study we want to evaluate 18F-FLT uptake and ADC as predictive imaging biomarkers of cell proliferation and cell death, respectively, using histopathology as the reference test.

Study objective

Primary objectives
* 18F-FLT-PET/CT:
- To correlate the percentage change in SUV between baseline (SUV-1) and early therapy (SUV-2) with pathological quantification (% of viable tumor cells) of the primary tumor after pre-operative chemotherapy in patients with operable NSCLC.

* DWI-MRI:
- To correlate the percentage change in ADC between baseline (ADC-1) and early therapy (ADC-2) with pathological quantification (% of viable tumor cells) of the primary tumor after pre-operative chemotherapy in patients with operable NSCLC.

2.2 Secondary objectives

* 18F-FLT-PET/CT:
- To demonstrate correlation between pre-operative SUV (SUV-3) and tumor proliferation marker Ki67 index in NSCLC.
- To compare the changes of SUV (SUV-3 vs. SUV-1; SUV-2 vs. SUV-1) to changes in tumor size from anatomic imaging (CT/MRI).
- To compare the changes of SUV (SUV-3 vs. SUV-1; SUV-2 vs. SUV-1) to metabolic changes from 18F-FDG-PET, if available.

* DWI-MRI:
- To compare the changes of ADC (ADC-3 vs. ADC-1; ADC-2 vs. ADC-1) to changes in tumor volume from anatomic imaging (CT/MRI).
- To compare the changes of ADC (ADC-3 vs. ADC-1; ADC-2 vs. ADC-1) to metabolic changes from 18F-FDG-PET, if available.

* Both 18F-FLT-PET/CT and DWI-MRI:
- To demonstrate correlation between ADC and SUV at the same time point.

Study design

This is a prospective, multicenter, single-arm imaging trial. Patients with NSCLC will undergo 18F-FLT-PET/CT and DWI-MRI scans on three separate occasions: at baseline, at 14 days (maximum +/- 1 days deviation is acceptable) after first administration of chemotherapy and finally after up to 4 cycles of chemotherapy. Dedicated in-house developed software will be used to quantify 18F-FLT SUV and ADC to assess tumor characteristics and response to therapy. And these measures will be compared to pathological quantifications of the primary tumor performed after resection.

Study burden and risks

A PET scan is a regular diagnostic imaging technique. Each study will be performed in complance with the radiation safety guidelines of the department. The total radiation dose will be 20.4 mSv. To compare, every person living in the Netherlands receives a natural background doses of 2-2.5mSv per year. Although the extra dose is relatively high we think that it is acceptable for this particular study in view of this specific population and high scientific impact. The 5-year overall survival rates for stage II and IIIA disease is 30% and 20% respectively, whereas the possible hazard of cancer induction by radiation is small and only after several years (>10 years). In addition the results of this study will have great clinical benefit in improving personalized therapy stragies for cancer patients. Cannulation of the venous canulla will be performed by experienced clinicians of the Department of radiology and nuclear medicine. In spite of this, occasionally these cannulae may cause a hematoma. Druing the study a maximum of 30 mL is taken (10 mL per FLT-scan).

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

* Age >= 18 years
* WHO performance status 0-1
* Histologically or cytological confirmed clinical stage II-IIIA non-small cell lung carcinoma (NSCLC), according to 7th TNM classification (NOTE: patients with resectable N2 disease are also eligible)
* Baseline standard imaging assessment & staging should be performed within 6 weeks prior to planned treatment start.
* Patients must be candidate for curative intent surgery, and must be expected to complete the treatment.
* No prior or current anticancer treatment for NSCLC, pre-operative therapy will include only chemotherapeutic drugs (pemetrexed is contraindicated), no other biological, targeted or radiotherapy is allowed

* No treatment with any investigational drug substance within 4 weeks prior to registration.
* No other malignancies in the 3 years prior to study entry with the exception of surgically cured carcinoma in situ of the cervix, in situ breast cancer, incidental finding of stage T1a or T1b prostate cancer, and basal/squamous cell carcinoma of the skin
* No evidence of any medical condition which would impair the ability of the patient to participate in the trial or might preclude therapy with chemotherapeutic drugs according to routine medical practice (e.g. unstable or uncompensated respiratory, cardiac, hepatic or renal disease, known dihydropyrimidine dehydrogenase deficiency, active infection, uncontrolled diabetes mellitus; uncontrolled arterial hypertension, history of unstable myocardial infarction)
* Adequate hematology and biochemical investigations, (should be done maximum 6 weeks before treatment starts)
* Normal bone marrow function based on routine blood samples, i.e. neutrophils >= 1.5 x 109/L, platelets >= 75 x 109/L, hemoglobin >= 10.0 g/dL
* Normal kidney function creatinine clearance >= 60 mL/min,
* Normal liver function assessed by routine laboratory examinations, i.e. bilirubin < 1.5 x upper limit of normal (ULN), ALT< 3 x ULN
* Patients must not have any contraindication for 18F-FLT-PET/CT or MRI procedures.
* Patient primary lung tumor larger than 20 mm in diameter (measured by diagnostic CT or MRI).
* Women of child bearing potential (WOCBP) must have a negative serum (or urine) pregnancy test before trial registration.
* Patients of childbearing / reproductive potential should use adequate birth control measures, as defined by the investigator, during the study treatment period and for at least 6 months after the last study procedure. A highly effective method of birth control is defined as those which result in low failure rate (i.e. less than 1% per year) when used consistently and correctly.
* Female subjects who are breast feeding should discontinue nursing before trial registration.
* Absence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before randomization in the trial.
* Before patient registration, written informed consent must be given according to ICH/GCP, and national/local regulations.

Exclusion criteria

- Does not meet the inclusion criteria
- Younger than 50 years

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):	13-04-2016
Enrollment:	4
Type:	Actual

Ethics review

Approved WMO

Date:	12-08-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL51780.029.14