The beneficial value of 18F FDG PET/CT in the follow-up of stage III non-small cell lung cancer patients

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Primary Objective The primary objective of this study is to compare the 3-year overall survival of stage III NSCLC patients during follow-up surveillance with 18F FDG PET/CT versus follow-up with conventional CT surveillance. Secondary...

Ethical review	Approved WMO
Status	Recruitment started
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional research previously applied in human subjects

Summary

ID

NL-OMON56590

Source
ToetsingOnline

Brief title
NVALT31-PET Study

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Lung cancer Lung carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Zorginstituut/ZonMW

Intervention

- Intervention with ionizing radiation

Keyword: (Cost)-effectiveness, Non-small cell lung cancer (NSCLC), Overall survival, PET scan

Explanation

N.a.

Outcome measures

Primary outcome

Overall survival (OS) will be defined as time from end of curative intent treatment until death or loss to follow-up or end of study defined as 3 years after end of curative treatment. OS will be recorded in the eCRF and cross-validated through a linkage with the National Cancer Registry. Primary analyses will be performed on an intention-to-treat basis. The secondary analyses will include per protocol analyses as well.

Secondary outcome

Recurrences, possible treatment after a recurrence, and event-free survival will be recorded in the eCRF, filled out by the Health Care Practitioners (HCP's) or a representative.
Health-related quality of life and cost-effectiveness will be investigated at baseline and every six months until 24 months of follow-up and then yearly until three years, using the following validated questionnaires: EORTC-QLQ C30, EORTC-LC13, the PRO-CTCAE lung cancer subset, EQ-5D-5L, Medical Consumption Questionnaire (iMCQ), and the Productivity Costs Questionnaire (iPCQ). Hospital resource use will be retrieved from the EHR, and will include all diagnostic testing, hospital visits, telephone consultations, email consultations and medical use known by the hospital.
The impact of the additional 18F FDG PET/CT scans in follow-up care on distress will be evaluated every six months until 24 months of follow-up and then yearly until three years, using the Cancer Worry Scale (CWS) and the Hospital Anxiety and Depression Scale (HADS). Semi-structured interviews with some patients will be conducted in the weeks after their 18F FDG PET/CT scans to to assess their experiences whether the (possible) benefits outweigh the burden of the additional 18F FDG PET/CT scan in their follow-up care (in terms of time and investment). To uniform the direction of the interviews, a semi-structured interview guide will be developed based on literature and the experience within the research team.
Some hospitals will participate in obtaining blood samples to assess the beneficial value of ctDNA in the detection of recurrences. For patients in the intervention group that give additional consent for collecting blood, three cell-free DNA tubes will be collected around every follow-up scan, when the IV is inserted or at a planned blood test. The tubes will subsequently be sent to the sponsor within 24 hours, where the cell-stabilizing tubes will be centrifuged at room temperature for 10 min at 1600 g. Cell-free plasma will be stored in 5 mL aliquots at 80 °C until DNA isolation. Cell-free DNA will be isolated from 1 ml plasma for mutation analysis.

Study description

Background summary

Stage III NSCLC patients are at high risk of developing recurrences (50-78%) during follow-up. With 18F FDG PET/CT, recurrence may be detected earlier at an oligometastatic state when curative-intent treatment is still possible. With the increasing availability of local therapeutic options for patients with oligometastatic disease, early detection of tumor recurrence is likely to prolong survival and health-related quality of life and thereby lower the disease burden. Currently, there are no clinical trials performed with the aim to demonstrate the potential beneficial effect of 18F FDG PET/CT in the follow-up of NSCLC patients. Furthermore, CT-based follow-up was introduced before the promising effects of adjuvant therapy and radical treatment in oligometastatic patients were available. These new therapies have significant benefits for patients and favor early detection of recurrences to be most efficacious in lowering the disease burden.

Study objective

Primary Objective The primary objective of this study is to compare the 3-year overall survival of stage III NSCLC patients during follow-up surveillance with 18F FDG PET/CT versus follow-up with conventional CT surveillance.
Secondary Objectives Unless otherwise stated follow-up refers to the three year follow-up period. The secondary objectives of this study are:

- - To compare the 2-year overall survival of stage III NSCLC patients during follow-up surveillance with 18F FDG PET/CT versus follow-up with conventional CT-based surveillance (interim analysis);
- To compare the number of detected (symptomatic and asymptomatic) recurrences of stage III NSCLC patients during follow-up surveillance with 18F FDG PET/CT versus follow-up with conventional CT-based surveillance;
- To compare the event-free survival of stage III NSCLC patients during follow-up surveillance with 18F FDG PET/CT versus follow-up with conventional CT-based surveillance;
- To determine the cost-effectiveness of 18F FDG PET/CT versus conventional CT-based surveillance during follow-up of stage III NSCLC patients;
- To compare the effect of 18F FDG PET/CT versus conventional CT-based surveillance on health-related quality of life during follow-up of stage III NSCLC patients;
- To assess stage III NSCLC patients' experiences of the additional 18F FDG PET/CT scan in their follow-up care;
- To assess the beneficial value of circulating tumor DNA (ctDNA) in the detection of recurrences during follow-up in stage III NSCLC patients;
- To assess differences in type of treatment following recurrence during follow-up in stage III NSCLC patients.

Exploratory Objectives The exploratory objectives of this study are to create a multimodal cohort in which we collect data to answer future additional research questions if funding

becomes available, e.g.:

- determining optimal timing of follow-up scans;
- creating a database with 18F FDG PET/CT and CT-scans to train and validate AI based algorithms for anomaly detection and thereby potentially improve sensitivity and specificity of those imaging modalities to detect recurrences and/or discriminate between recurrences and new primary tumors.
- long-term overall survival (>3 years after end of curative intent treatment)

Study design

We will perform a multicenter randomized controlled clinical trial with a superiority design. At the start of follow-up care, patients will be randomized 1:1 to either the intervention (18F FDG PET/CT) or the control group (care as usual, CT-based follow-up). Randomization will be done stratifying for histology (squamous vs non-squamous), and treatment (chemo radiation only vs. (concurrent or sequential) chemo radiation with (neo-)adjuvant immunotherapy vs. radiotherapy only vs. resection (with or without (neo-)adjuvant treatment).

Intervention

Intervention:
The intervention group (n = 345) consists of usual care until 3 years of follow-up (see control group) with additional whole-body 18F FDG PET/CT scans (from the skull to, at least, the midfemoral region) during follow-up visits at 6 months, 12 months, 18 months, 24 months, and 36 months of follow-up (range 2 months). After the 36-month follow-up period, patients will receive follow-up usual care (i.e. CT-scans).

Control group:
The control group (n = 345) consists of regular follow-up visits with physical check-ups and CT-scans at least every 6 months for the first 2 years and then at least yearly CT-scans until 3 years of follow-up. In case of suspected recurrence/metastasis or inconclusive results of a CT-scan (eg, after radiotherapy), 18F FDG PET/CT should be considered.

Study burden and risks

The usual care CT-scans will be complemented by 18F FDG PET/CT scans in the intervention group. The radiation doses and the 18F FDG PET/CT scan will be according to intended use and CE approval. Potential risks for some patients in the intervention group may be an immediate allergic infusion reaction to iodinated contrast agent and/or complications from venous cannulations. However, these risks are deemed acceptable for patients suffering from cancers in relation to benefits obtained from this study, i.e. resulting in detection of tumor recurrence at an oligometastatic state or second primary lung cancer where curative-intent treatment is still possible. Early detection of tumor recurrence is likely to prolong survival and health-related quality of life and
thereby lower the disease burden.
The extra burden for patients consists of the extra time of the 18F FDG PET/CT scan (approx. 2 hours per scan) and the extra time all patients will spend (approx. 45 min) on completing

the questionnaires at the six time points. Optionally, patients from the intervention group can participate in an evaluation interview and/or the blood collection. Potential risk for the participating patients is classified as low.

Contacts

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Trial sites

Trial sites in the Netherlands

Radboud Universitair Medisch Centrum
Target size: 30

Amsterdam UMC
Target size: 30

Diakonessenhuis Utrecht
Target size: 34

Dijklander Ziekenhuis
Target size: 40

Deventer Ziekenhuis
Target size: 20

Elisabeth-Tweesteden ziekenhuis
Target size: 40

Groene Hart Ziekenhuis
Target size: 20

HagaZiekenhuis
Target size: 20

Medisch Spectrum Twente
Target size: 13

Tergooiziekenhuizen locatie Hilversum
Target size: 10

Treant Zorggroep
Target size: 30

Antoni van Leeuwenhoek (AVL)
Target size: 30

Universitair Medisch Centrum Utrecht
Target size: 8

Maxima Medisch Centrum
Target size: 15

GelreZiekenhuizen
Target size: 25

Martini Ziekenhuis
Target size: 30

St. Antonius Ziekenhuis
Target size: 10

Franciscus
Target size: 30

Bravis Ziekenhuis
Target size: 54

Haaglanden Medisch Centrum (HMC)
Target size: 8

Nij Smellinghe Ziekenhuis
Target size: 10

Streekziekenhuis Koningin Beatrix
Target size: 15

Canisius Wilhelmina Ziekenhuis
Target size: 40

Tjongerschans
Target size: 10

Maasstadziekenhuis
Target size: 23

Ziekenhuisvoorzieningen Gelderse Vallei
Target size: 30

Amphia Ziekenhuis

Target size: 30

OLVG
Target size: 35

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Cytological or histologically proven stage III non-small cell lung cancer before start of curative intent treatment
• Treated with curative intent and started follow-up care
• All adjuvant treatments are permitted as co-intervention during follow-up care
• Age 18 years or older
• ECOG Performance Status classification 0-2 at moment of inclusion
• Written and signed informed consent by the patient or their representative (with the understanding that consent may be withdrawn by the patient or their representative at any time without consequences to future medical care)

Exclusion criteria

• Life expectancy shorter than 6 months at the end of curative intent treatment
• Evidence of recurrence after end of curative intent treatment and before randomization (4 months follow-up)
• Any condition that, in the opinion of the investigator, would interfere with evaluation of the intervention or interpretation of HRQOL or other study results.

Study design

Design

Study phase:	N/A
Study type:	Interventional research previously applied in human subjects
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	No intervention
Primary purpose:	Health services research

Recruitment

NL

Recruitment status:	Recruitment started
Start date (anticipated):	19-03-2024
Enrollment:	690
Duration:	32 months (per patient)
Type:	Actual

Medical products/devices used

Product type:	N.a.
Registration:	No

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N.a.

Ethics review

Approved WMO Date:	08-01-2024
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-02-2024

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-04-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-05-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-06-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-11-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-03-2025
Application type:	Amendment
Review commission:	METC Oost-Nederland
Notification accepted Date:	17-05-2025
Application type:	Amendment
Review commission:	METC Oost-Nederland
Approved WMO Date:	03-06-2025
Application type:	Amendment
Review commission:	METC Oost-Nederland

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
ClinicalTrials.gov	NCT06082492
CCMO	NL83288.091.23
Research portal	NL-007304