Early response evaluation of proton therapy by PET-imaging in squamous cell carcinoma located in the head and neck

Published: 30-03-2018
Last updated: 12-04-2024

Objective: To assess whether early changes in hypoxia between baseline and in the (end of the) second week of proton therapy are predictive for time-to-local recurrence in patients with HNSCC (primary). Secondary objectives include: to compare the...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON52797

Source
ToetsingOnline

Brief title
ERM-PT-HNSCC

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
'head-and-neck cancer', 'head-and-neck squamous cell carcinoma'

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: ZonMW (Vernieuwingsimpuls;Veni)

Intervention

Keyword: hypoxia, PET-CT, proton therapy, response-evaluation

Outcome measures

Primary outcome

Main study parameters/endpoints: The main study parameters are the percent change in hypoxic tumour volume between baseline PET and interim PET of hypoxia. The primary endpoint is 3-year local recurrence-free survival (LRFS).

Intervention: All patients are asked to undergo one additional baseline 18F-FAZA PET-scan (hypoxia) at baseline 18F-FDG PET-imaging (glucose metabolism) is already performed during clinical work-up. Both 18F-FAZA and 18F-FDG PET-scans will be repeated in the (end of the) second week of PT, unless no hypoxia is witnessed at baseline, then only the 18F-FDG PET-scan is repeated. In a pilot setting, 10 patients are asked to further undergo activation PET-scanning immediately after PT in the first, second and last week.

Secondary outcome

To assess whether early changes in glucose metabolism between baseline and the second week of PT are predictive for time-to-local recurrence after PT for HNSCC.

To assess independent predictive value of, and preference for either (baseline, interim or changes in) hypoxia-PET or PET of glucose metabolism (in whom and when);

To assess spatial conformity of recurrences with PET-identified radioresistant

areas (where) in relation to planning dose and accuracy of dose-delivery;

To perform adaptive replanning based on two-timepoint PET and determine the

expected dose to tumour and normal tissues for each PET technique;

To assess spatial conformity of treatment plan and dose-delivery determined by

activation PET using a clinical scanner (quality assurance);

To determine tissue-changes during PT measured by activation PET and relate

these to the study endpoint and PET of glucose metabolism and hypoxia.

Study description

Background summary

Rationale: Proton therapy (PT), currently being introduced in the Netherlands, delivers radiation dose more conformal than photon radiotherapy, therefore healthy tissue damage is expected to be lower and at least similar tumouricidal effects are described. This increases the therapeutic window of radiotherapy which could be used for intensified treatment to patients prone to locoregional failure. From photon radiotherapy it is known that stratification of patients with head and neck squamous cell carcinoma (HNSCC) is possible using different positron-emission tomography (PET-)techniques. Distribution of tumour hypoxia, a main cause of resistance to radiotherapy, and glucose metabolic need have been described. PT, in contrast to photon therapy, results in activation of endogenous atoms in the irradiated tissues which can be measured using PET and reflect dose deposition and tissue composition. This provides a unique application of PET in this treatment modality as quality assurance of proton therapy and potentially as biomarker of tissue response to proton therapy. The main hypothesis is that early during PT, PET is capable of discerning a subset of patients with increased risk of locoregional failure with a univariate hazard-ratio of at least 4.0. At this time point, treatment intensification would still be possible.

Study objective

Objective: To assess whether early changes in hypoxia between baseline and in the (end of the) second week of proton therapy are predictive for time-to-local recurrence in patients with HNSCC (primary). Secondary objectives include: to compare the role of hypoxia-PET to more readily available PET of glucose metabolism, to describe spatial conformity between the PET-scan and the

location of the recurrence, to determine the potential of adaptive replanning based on two-timepoint PET-imaging. In a pilot setting the feasibility of activation PET in a clinical setting for quality assurance of PT-plans and potential biomarker of PT-induced tissue changes will be explored.

Study design

Study design: Prospective, single-arm, observational cohort study with invasive measurements.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Each PET-acquisition will be performed in radiotherapy position preferably using fixation devices (mould mask). The procedures of PET-imaging of 18F-FAZA (hypoxia) and 18F-FDG (glucose metabolism) each involve preparation (hypoxia: none, glucose metabolism: 6h fasted), intravenous injection of a radiopharmaceutical, a waiting period in solitude (hypoxia: 2 h, glucose metabolism: 1 h), followed by PET-acquisition (hypoxia: 10-20 min, glucose metabolism: 5-10 min). Occurrence of infusion-related reactions (e.g. allergy) is unlikely. The radiation burden attached to each of these procedures are 6.8 mSv (hypoxia) and 2.9 mSv (glucose metabolism). The pilot substudy requires immediate transfer from PT-gantry to scanner followed by a 30-min PET-acquisition, three times, resulting in a radiation burden of ~0.5 mSv per procedure. All other procedures are part of clinical protocol. There will be no individual benefit for enrolled subjects. Financial compensation for study-related travel expenses have been arranged. However, where possible, each study procedure will be combined with a regular visit to the PT-facility.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

protocol "inclusion criteria" (paragraph 4.2.1).
- adult
- primary untreated head-and-neck squamous cell carcinoma
- measurable lesion of at least 2 cm diameter
- eligible for protontherapy ± chemotherapy at HollandPTC
- expected life expectancy at least 3 months

Exclusion criteria

protocol "exclusion criteria" (paragraph 4.2.2).
- known metastases
- paranasal sinus, salivary or thyroid cancer
- prior chemotherapy or radiotherapy within last 3 years
- resected disease
- concurrent malignancies
- uncontrolled diabetes mellitus

Study design

Design

Study type: Observational invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-03-2021
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	30-03-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	24-04-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	04-02-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	21-03-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NCT03513042
CCMO	NL63825.058.17