Non invasive imaging of [18F]HX4 with Positron-Emission-Tomography (PET) in Head and Neck Cancer.

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Non invasive imaging of hypoxia with the aid of PET-scans could help to select the patients having a hypoxic tumor who could be treated with specific anti-hypoxic treatments. The added value of additional anti-hypoxic treatments depends on the...

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

Summary

ID

NL-OMON39184

Source
ToetsingOnline

Brief title
PET with [18F]HX4

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Cancer of the Head and Neck, Squamous cell carcinomas of head and neck

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: The Center for Translational Molecular

Medicine (CTMM) en Metoxia

Intervention

Keyword: [18F]HX4, Cancer of the Head and Neck, hypoxia, PET

Outcome measures

Primary outcome

Visualisation of tumor hypoxia with [18F] HX4 PET imaging

Secondary outcome

- Observe spatial and temporal stability of [18F] HX4 PET images

- Correlation of [18F] HX4 with local tumor recurrence and survival.

- Image quality of [18F] HX4-PET at different time points

- Kinetic analysis of HX4

- Correlation of hypoxia imaging with blood hypoxia markers (osteopontin, circulating CA-IX)

- Correlation of hypoxia imaging with tumor tissue biomarkers (HPV, CA-IX, VEGF, EGFR, CD44, HIF-1*, mir-210) and autophagy related genes.

- Spatial correlation of [18F] HX4-PET with [18F] FDG PET pre-treatment

- Spatial correlation of [18F] HX4-PET with [18F] FDG PET three months after treatment

- Determine SUVmax and target-to-background ratio in the [18F] FDG and [18F] HX4 images within atherosclerotic carotid plaque(s) before, during, and after radiation therapy.

- Correlation of the SUVmax and the target-to-background ratio in the [18F]FDG and [18F]HX4 images with artherosclerotic plaque components on diagnostic CT.

Study description

Background summary

Tumor hypoxia is the situation where tumor cells have been deprived of oxygen. Hypoxic tumor cells are usually more resistant to radiotherapy and chemotherapy and more likely to develop metastasis3,4
Tumor oxygenation is frequently measured with an Eppendorf electrode. This is an invasive procedure, limiting its application in clinical practice. Measuring tumor hypoxia by non-invasive methods includes the use of bioreductive markers, such as the 2-nitro-imidazole derivatives. These 2-nitroimidazoles are known to be metabolically reduced and trapped within hypoxic cells. Based on this mechanism of action they have been investigated extensively as a radio-sensitizer5. The selective binding and retention of 2-nitroimidazoles in hypoxic regions offers significant potential for one or more labelled nitroimidazoles to emerge as a clinically useful non-invasive hypoxia markers. The 2 nitroimidazole nucleoside analogue HX4 was developed as a potential radio-sensitizer for hypoxic tumor cells6. In a recent phase 1 clinical study from van Loon et al 1, PET-imaging with [18F]HX4 was feasible without any toxicity. In head and neck cancer tumor hypoxia is known to be an important prognostic factor for long term survival7. To define the added value of anti-hypoxic therapies in this patient population, an estimation of the proportion of tumors with hypoxia is essential. In previous research, 18F-fluoromisonidazole (18FMISO) was able to detect hypoxia in 71-87% of patients with head and neck squamous cell carcinoma8-10. In this observational imaging trial these results will be verified by hypoxia imaging with [18F]HX4.

Study objective

Non invasive imaging of hypoxia with the aid of PET-scans could help to select the patients having a hypoxic tumor who could be treated with specific anti-hypoxic treatments. The added value of additional anti-hypoxic treatments depends on the amount of patients who will benefit from them. Several 2-nitroimidazoles, labelled with Fluor-18 (18F) have already been used in patients to identify hypoxia. However, suboptimal image quality and unpredictable kinetics limit their use. In extensive pre-clinical models and a clinical phase 1 study the combination of HX4 labelled with 18F showed to be a promising and non-toxic new probe to determine hypoxia. With this tracer the proportion of hypoxic tumors in head and neck cancer patients will be verified.

The aim of this study is to determine if tumor hypoxia can be accurately visualised with [18F] HX4 PET imaging in head and neck tumors.

Study design

Phase II, single-centre imaging, non-randomized, open-label trial

Intervention

Fluor-18 labelled HX-4 (444MBq, 27 *g HX-4)

Study burden and risks

All patients will be monitored carefully during and after administration of the labelled [18F]HX4 by trained caregivers. The proposed [18F]HX4 dose is chosen based on the phase 1 study with [18F]HX41. In view of previous experiences with [18F]HX4, conventional PET-CT and other nitroimidazole drugs, we expect no unforeseen side effects.

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

- Histological or cytological confirmed HNSSC of the oral cavity, oropharynx, hypopharynx, larynx, T2-T3-T4, any N, M0;- Tumor (or lymph node) diameter * 2,5 cm;- WHO performance status 0 to 2;- Scheduled for primary curative (concurrent chemo-) radiotherapy;- No previous surgery to the head and neck;- No previous radiation to the head and neck;- Adequate renal function (calculated creatinine clearance at least 60 ml/min) ;- The patient is willing and capable to comply with study procedures;- 18 years or older;- Have given written informed consent before patien registration

Exclusion criteria

No recent (< 3 months) myocardial infarction;- No Uncontrolled infectious disease;- Not pregnant or breast feeding and willing to take adequate contraceptive measures during the study

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-12-2011
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Radiolabeled HX4 with 18 Fluor

Generic name:	-

Ethics review

Approved WMO Date:	11-11-2011
Application type:	First submission
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	25-11-2011
Application type:	First submission
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	23-09-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-10-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	03-06-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	04-07-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
EudraCT	EUCTR2011-001812-80-NL
ClinicalTrials.gov	NCT01347281
CCMO	NL37084.068.11