Non invasive imaging of tumor hypoxia with [18F]HX4 Positron-Emission-Tomography (PET): A phase II trial

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Primary Objective: Visualization and quantification of tumor hypoxia with [18F] HX4 PET imagingSecondary Objectives: - Correlation of [18F] HX4 with local tumor recurrence and survival- Correlation of hypoxia imaging with blood hypoxia markers -...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON44468

Source
ToetsingOnline

Brief title
HX4 several disease

Condition

- Other condition
- Malignant and unspecified neoplasms gastrointestinal NEC
- Reproductive neoplasms male malignant and unspecified

Synonym
cancer: several diseases

Health condition

hersenen, primaire maligne glioom of metastasen

Research involving

Human

Sponsors and support

Primary sponsor: MAASTRO Clinic
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: [18F]HX4, cancer, PET, phase II trial

Outcome measures

Primary outcome

Tumor to background ratio of [18F] HX4 PET images.

This endpoint will be evaluated approximately 3 months after inclusion of all patients

Secondary outcome

- Correlation of the SUVmax, SUVmean, SUVpeak and tumor to background ratio in the [18F] HX4 PET images in comparison to local tumor recurrence and survival.
- Determine if there is a relationship between the SUVmax, SUVmean, SUVpeak or tumor to background ratio in comparison to blood or tissue biomarkers.
- Overlap fraction of (for example) >50% max regions between HX4-PET and FDG-PET pre-treatment or three months after treatment.
- Quantitative and qualitative correlation of [18F] HX4-PET obtained before treatment and two weeks into treatment

These secondary endpoints will be evaluated 2 years after the inclusion of all patients, since we want correlate hypoxia PET imaging to (at least) 2-year

overall survival.

Study description

Background summary

Regulation of tissue oxygen homeostasis is critical for cell function, proliferation and survival. Evidence for this continues to accumulate along with our understanding of the complex oxygen-sensing pathways present within cells. Several pathophysiological disorders are associated with a loss in oxygen homeostasis, including heart disease, stroke, and cancer. The microenvironment of tumors in particular is very oxygen heterogeneous, with hypoxic areas which may explain our difficulty treating cancer effectively.

Prostate carcinomas are known to be hypoxic. Increasing levels of hypoxia within prostatic tissue is related to increasing clinical stage, patient age and a more aggressive prostate cancer.
Several researches indicated that hypoxia might also play a role in esophageal cancer.
In glial brain tumors, hypoxia is correlated with more rapid tumor recurrence and the hypoxic burden in newly diagnosed glioblastomas is linked to the biological aggressiveness.
In brain metastases CA-IX expression (a marker for hypoxia) is correlated to the primary non-small cell lung carcinomas.
Hypoxia enhances proliferation, angiogenesis, metastasis, chemoresistance and radioresistance of hepatocellular carcinoma.
The hypoxic markers HIF-1*, VEGF, CA-IX and GLUT-1 were all over expressed in colorectal cancer and its liver metastases.

Based on literature, hypoxia in tumors originating or disseminated to prostate, esophagus, brain and rectum cancer will be studied in this trial.

Hypoxia can be measured in several ways.
Radio-labelled nitroimidazoles offer significant potential to emerge as clinically useful non-invasive hypoxia markers.
The 2-nitroimidazole nucleoside analogue, 3-[18F]fluoro-2-(4-((2-nitro-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazol-1- yl)propan-1-ol ([18F]HX4) was developed to achieve better water solubility and faster clearance than most known nitro-imidazoles and is therefore expected to have better pharmacokinetic properties.

Study objective

Primary Objective:

Visualization and quantification of tumor hypoxia with [18F] HX4 PET imaging

Secondary Objectives:
- Correlation of [18F] HX4 with local tumor recurrence and survival
- Correlation of hypoxia imaging with blood hypoxia markers
- Correlation of hypoxia imaging with tumor tissue biomarkers
- Evaluation of tumor hypoxia changes during treatment.
- Spatial correlation of [18F] HX4-PET with imaging pre-treatment (if present from routine clinical practice)
- Spatial correlation of [18F] HX4-PET with imaging three months after treatment (if present from routine clinical practice)

Study design

A non-randomized, open label trial.

Eligible patients with histologically/cytologically proven primary tumors of the prostate, esophagus, brain or rectum or metastatic disease to the brain (originating from breast, lung or colorectal).

Before treatment
A baseline [18F]HX4 PET scan will be performed, by administrating 444 MBq (12 mCi) [18F]HX4 via a bolus IV injection. The PET/CT scan is acquired at 4 hours p.i.* A blood sample is drawn to measure hypoxia-related proteins in the blood.

Treatment
The cancer treatment will not be changed by this study and will be performed according to local guidelines. Radiotherapy will consist of a fractionated schedule (combined with , e.g., chemotherapy or hormonal therapy) or of stereotactic ablative (body) radiotherapy.

During treatment
If patients are treated with radiotherapy and/or chemotherapy the [18F]HX4 scan (4h p.i.) will be repeated after 2 weeks of radiotherapy, by administrating 444MBq (12mCi) [18F]HX4 via a bolus IV injection. For prostate patients treated with HDR brachytherapy an alternative timepoint is chosen: the HX4 scan during treatment will be performed 4 weeks after HDR treatment.

Follow up
In some patients treated with radiotherapy only or chemoradiotherapy [18F]FDG PET scan three months after the end of treatment will be acquired if part of routine clinical practice. Clinical follow-up will take place according to routine clinical practice at the outpatient clinic.

This study will cause no delay in the anticancer treatment.

* After 3 patients (of each tumor type) a feasibility evaluation will be

performed.
*

Study burden and risks

Based on current information, there are no adverse events anticipated in relationship to the administration of [18F]HX4. However, the possibility of commonly experienced mild side effects related to other components of the investigational product or the PET-CT imaging procedure, such as bruising at the IV site, may be anticipated.

The radiation burden due to [18F]HX4 is similar to that encountered in many routine nuclear medicine procedures e.g. 18FDG PET. Administration of [18F]HX4 presents no known risks. In previous studies (healthy volunteers, phase I, phase II) no adverse effects were observed. Radiation dosimetry estimates for [18F]HX4 indicate that the radiation dose is similar to other radiodiagnostic agents and does not represent any undue risk. Moreover, no delay of anti-cancer therapy is required.

There are no immediate potential benefits except the satisfaction to participate to improve of knowledge. Early research indicates that [18F]HX4-PET imaging may provide the benefit to, non-invasively, assist in measuring tumor hypoxic fraction in human tumors. It provides a tool that could offer sufficient potential to improve cancer therapy.

Contacts

Public
MAASTRO Clinic

Dr. Tanslaan 12
Maastricht 6229 ET
NL
Scientific
MAASTRO Clinic

Dr. Tanslaan 12
Maastricht 6229 ET
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet the general and tumor site specific criteria:;General:
- Histological/cytological confirmed carcinoma of de esophagus, rectum or prostate or radiological suspicion for Grade IV glioma (primary brain tumor) or brain metastases.
- WHO performance status 0 to 2.
- 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 patient registration;Prostate
- Histological confirmed prostate tumor
- High grade tumor (Gleason score *8)
- Macroscopically visual tumor on MRI
- Tumorload based on biopsy > 25%
- No previous surgery of the prostate.
- No previous radiotherapy of the prostate
- No previous chemotherapy or hormonal therapy;Esophagus
- Histological or cytological confirmed adenocarcinoma of the esophagus
- Tumor diameter * 2,5 cm
- No previous surgery to the esophagus
- No previous radiotherapy of the esophagus.
- No previous chemotherapy.;Primary brain tumor (Grade IV glioma)
- Suspected grade IV glioma on magnetic resonance imaging
- Macroscopically visual tumor on MRI (diameter larger than 2 cm)
- No previous radiotherapy, chemotherapy or surgery;Brain (metastases)
- Raiological suspicion for brain metastases:macroscopically visual tumor on MRI (diameter larger than 2 cm and suitable for SBRT)
- Planned for curative treatment with stereotactic body radiotherapy (SBRT);Rectum
- Histologically confirmed rectum tumor
- Tumor size length * 2,5 cm
- Eligible for long-course radiochemotherapy
- No previous surgery or radiotherapy of the rectum
- No previous chemotherapy

Exclusion criteria

- Recent (< 3 months) myocardial infarction;- 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):	11-10-2016
Enrollment:	120
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Radio-labelled HX4 with 18 Fluor
Generic name:	[18F]HX4

Ethics review

Approved WMO

Date:	17-06-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	09-07-2015
Application type:	First submission
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	EUCTR2014-003873-41-NL
CCMO	NL50833.068.14