Evaluation of bone marrow hypoxia with 18F-FAZA PET in patients with relapsing multiple myeloma; a pilot study

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This pilot study will evaluate whether tumour hypoxia can be demonstrated in the bone marrow compartment of relapsing MM patients by using the tracer 18F-FAZA. The results will be compared with the results of the FDG-PET scan. In addition in vitro...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Plasma cell neoplasms
Study type	Observational invasive

Summary

ID

NL-OMON35390

Source
ToetsingOnline

Brief title
F-FAZA MM

Condition

- Plasma cell neoplasms
- Bone disorders (excl congenital and fractures)

Synonym
Multiple myeloma and Kahler's disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: FDG-PET, F-FAZA, Hypoxia, Multiple myeloma

Outcome measures

Primary outcome

Feasibility of 18F-FAZA scans in patients with relapsing multiple myeloma. In addition bone marrow staining to demonstrate whether hypoxia related proteins are upregulated by plasma cells or surrounding cells including HIF 1α , HIF2α , GLUT-1 and -3 and VEGF.

Secondary outcome

not applicable.

Study description

Background summary

1. Multiple myeloma and imaging techniques
Multiple Myeloma (MM) is clonal B cell disorder characterised by a monoclonal plasma cell population in bone marrow, with bone pain, anemia, hypercalcaemia, and kidney dysfunction as clinically presenting symptoms. In the majority of the patients the disorder is disseminated through the bone marrow compartment. The abnormalities of the skeleton can be identified by X-ray examination and demonstrates frequently the characteristics osteolytic defects. Following treatment with chemotherapy or radiotherapy the osteolytic defects persist and no clear distinction can be made whether vital tumour cells persist in these lesions. Also in relapsing disease the X-ray examination has a limited value unless progressive defects are observed. Therefore alternative scanning methods have been developed to visualize the emergence of new malignant plasma cells that make use of tracers that identify tumour-specific receptors of identify enhanced metabolic activity of the malignant plasma cells. Recently it was shown that FDG-PET can demonstrate more abnormal lesions in relapsing MM than whole body X-ray.

2. Tumour hypoxia
However the cause of the increased FDG-uptake is unclear. It might be related to inappropriate tumour out-growth or as a consequence of tumour hypoxia due to

inappropriate blood supply. Alternatively the glycolytic pathway might be installed due to malignant transformation. Recently we showed that the transcription factor STAT5 up regulates hypoxia inducing factor (HIF)-2 and as consequence an upregulation of genes involved in glucose up-take. Based on these findings it is unclear so far whether the enhanced metabolic activity defined by FDG-PET is related to hypoxia. There is evidence that HIF1α and HIF2α can be upregulated in plasma cells and thereby triggering the VEGF pathway. Other hypoxia related proteins like glucose transporter (GLUT)-1 and -3 can be co-expressed with HIF1α.

3. 18F-FAZA scanning
Recently new scanning methods have been developed for demonstrating in vivo tumour hypoxia. The developed PET tracer hypoxia, 1-α-D:
-(5-deoxy-5-[18F]-fluoroarabinofuranosyl)-2-nitroimidazole (18F-FAZA), has been shown to accumulate in experimental models of tumour hypoxia. In a study performed by Postema et al in 50 patients with different types of malignancy it was shown that the used in vivo scanning method is feasible and save in patients for showing in vivo hypoxia in a variety of tumour categories.

Study objective

This pilot study will evaluate whether tumour hypoxia can be demonstrated in the bone marrow compartment of relapsing MM patients by using the tracer 18F-FAZA. The results will be compared with the results of the FDG-PET scan. In addition in vitro staining of bone marrow material will be performed to demonstrate whether hypoxia related proteins are upregulated by plasma cells or surrounding cells including HIF 1α , HIF2α , GLUT-1 and -3 and VEGF.

Study design

This is a pilot-study, thus no formal group size calculation can be given. For the purpose of this study, 10 patients will be included. It is expected that this number will cover the variability of 18F-FAZA uptake of MM patients. Currently, the total number of patients fulfilling the eligibility criteria of this study is 20-30 on a yearly basis.

Study burden and risks

Burden or risk:
- Hematoma at the intraveneus injection site.
- Radiation dose of 5.6 mSv.

Benefit:
more information about the skeletal lesions of the patient.

Contacts

Public
Selecteer

Hanzeplein 1
9713 GZ groningen
NL
Scientific
Selecteer

Hanzeplein 1
9713 GZ groningen
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patient with a positive FDG-PET scan.
Patients with relapsing multiple myeloma according to international defined guidelines.;Relapse after having achieved complete remission.
1. Reappearance of paraprotein
2. More than 5% plasma cells in bone marrow.
3. New lytic lesions or progression of old lesions.
4. New hypercalceamia.;Relapse after having achieved partial remission
1. Increases of paraprotein with more than 25%
2. Increase of urine paraprotein with more than 25%
3. Increase of plasma cells in bone marrow with 10%
4. New lytic lesions or progression of old lesions
5. New hypercalceamia

Exclusion criteria

- Radiotherapy in the last 3 months.
- Ineligible to lay supine during the PET scan.
- Age <=18 years.
- Pregnancy.
- Claustrophobia
- Severe kidney dysfunction; serum-creatinine >=250 µM.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-09-2011
Enrollment:	10
Type:	Anticipated

Ethics review

Approved WMO

Date:	23-11-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL37437.042.11