FDHT-PET to visualize the effect on the androgen receptor level by bicalutamide

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Feasibility to detect a difference in uptake on 18F-FDHT scan after 4 weeks of treatment with bicalutamide in metastatic breast cancer patients.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON47891

Source
ToetsingOnline

Brief title
bicalutamide and FDHT PET in metastatic breast cancer patients

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
metastatic breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: persoonlijk budget hoofdonderzoeker

Intervention

Keyword: bicalutamide, breast cancer, FDHT, PET

Outcome measures

Primary outcome

The percentage difference in 18F-FDHT uptake in tumor lesions after 4 weeks of monotherapy bicalutamide. A minimum decrease of 20% in 18F-FDHT uptake after 6 weeks compared to baseline uptake, with an alpha of 0.05 and a power of 80%, is considered clinical significant.

Secondary outcome

The difference in change in 18F-FDHT uptake after 4 weeks between those patients with a response and those without response.

Relation of AR-expression and 18F-FDHT tracer uptake.

Relation of change in AR availability and different subgroups (i.e. luminal A, luminal B, triple negative).

Study description

Background summary

Metastatic breast cancer patients are eligible for hormone therapy when the hormone receptor is present at the tumor site. It is known that hormone status can change in the course of time. Obtaining biopsies to explore this issue, however, might not always be feasible due to patient or tumor characteristics, nor being patient friendly. Furthermore, a single biopsy from a metastatic lesion could not be representative for the patient*s hormone receptor status. It is likely that only those patients expressing the androgen receptor can benefit from androgen receptor targeting therapies such as bicalutamide. Given the effects of anti androgens with respect to binding to the AR whole body imaging of AR-expression with FDHT-PET gives various opportunities. First of all imaging and quantification of available AR binding sites before start of therapy, may be predictive of therapy response, as has been shown for other endocrine agents. Second, FDHT-PET during therapy can only show tracer uptake in residual ARs that are not blocked by the anti androgen therapy. In theory, only these receptors (that still show tracer uptake) can cause continued androgen-dependent signalling. FDHT-PET at baseline and during therapy can

therefore potentially give valuable information about the presence of residual AR binding sites in relation to dosing of drugs targeting the AR. The purpose is to evaluate whether non-invasive in vivo imaging of AR presence in metastatic breast cancer patients by means of FDHT-PET can be used to predict (early) treatment response to, and optimal dosing of, the antiandrogen bicalutamide. The ultimate goal is to contribute to optimal selection of breast cancer patients for antiandrogen treatment.

Study objective

Feasibility to detect a difference in uptake on 18F-FDHT scan after 4 weeks of treatment with bicalutamide in metastatic breast cancer patients.

Study design

This is a single arm, one stage feasibility study, which will be executed in the University Medical Centre Groningen, The Netherlands. The primary endpoint of the study is to evaluate the difference in 18F-FDHT uptake in tumor lesions after 4 weeks of bicalutamide treatment in 20 patients with AR-positive metastatic breast cancer. At day 0 before start with bicalutamide, a 18F-FDHT-PET/CT will be performed, and one after 4 weeks. The second 18F-FDHT-PET -PET will be performed to determine if this scan can be used as a biomarker for early response. No effect of 18F-FDHT on bicalutamide effect is expected in view of the short half life and very low dosage of the tracer. Patients will be treated with bicalutamide until progression or unacceptable toxicity is encountered.

Intervention

All patients will receive a baseline FDHT-PET scan and start with bicalutamide treatment 150mg daily. During follow-up patients will receive one FDHT-PET scan after 4 weeks. Treatment with bicalutamide will continue until progression or unacceptable toxicity is encountered.

Study burden and risks

In a phase 2 clinical trial with advanced breast cancer patients, the tolerability of bicalutamide in women was similar to that reported in men with prostate cancer and showed a clinical benefit rate of 6 months in 19% of the AR positive breast cancer patients.For patients participating in this study, the scan result will not affect standard clinical treatment decisions. Therefore, no benefit or adverse effect is to be expected in this setting for the present patients. For future patients, the scan might support optimal selection of patients for treatment.

For this study the patients will make 3 extra visits to the clinic. After

screening procedure (visit 1) is accomplished, patients will visit for an early treatment evaluation (visit 2) and after 4 weeks an FDHT-PET (visit 3). After these extra visits patients will be followed up as regular procedure.

Radiation burden: For a typical injection of 200 MBq the total radiation burden is 3.6 mSv. The diagnostic bone scan and CT-scan are performed as part of standard clinical (re-)staging and will therefore not add additional radiation that would otherwise not have been received by the patient. A low dose CT, performed with the PET-scan for attenuation correction, will lead to an additional 1.5 mSv.

Until now no side effects of 18F-FDHT have been registered.

Venous blood collection: additional samples will be taken on the same day as the PET scan, to determine hormone levels. This can be drawn from the infusion site and will therefore not add additional discomfort.

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

1. A history of histological proven AR-positive (i.e. >10% staining), HER2-negative metastatic breast cancer (preferably assessment on fresh metastasis biopsy, alternatively archival metastasis biopsy)
2. Tumor progression after at least one line of systemic treatment
3. Measurable disease according to RECIST 1.1; or evaluable disease
4. Age * 18 years
5. Postmenopausal status defined as one of the following:
* Age *60 years
* Previous bilateral oophorectomy
* Age <60 years and amenorrhea for >12 months in the absence of interfering hormonal therapies (such as LH-RH agonists and ER-antagonists
* Age <60 years using ER antagonists should have amenorrhea for >12 months and FSH >24U/L and LH>14U/L
6.Adequate hematological, renal and liver function as follows:
*Absolute neutrophil count >1.5 x 109/L
*Platelet count >100 x 10^9/L
* White blood cell count >3 x 10^9/L
*AST and ALT <5.0 x upper limit of normal (ULN)
*Creatinine clearance >50mL/min
*Protrombin time, partial tromboplastin time and INR <1.5 x ULN
7. Written informed consent

Exclusion criteria

1.Unable to comply with the protocol
2.Evidence of symptomatic central nervous metastases
3.Presence of life-threatening visceral metastases
4.Corrected QT interval (QTc) >500millliseconds at screening
5.Recent history of cardiac disease, including myocardial infarction, unstable angina pectoris or uncontrolled arrhythmia within 6 months prior to screening; or evidence of severe congestive heart failure with New York Heart Association severity classification > class I.
6.Recent history of trombo-embolic events within 6 months prior to screening
7.Hepatic impairment (Child-Pugh Class B or C)
8.Severe concurrent disease, infection, co morbid condition that, in the judgment of the investigator would make the patient inappropriate for enrollment
9.The concomitant use of strong CYP3A4 inhibitors (see table 1)
10.Previous anti-androgen treatment
11.Concurrent use of ER-directed anti hormonal therapies

12.Toxicity of radiotherapy or major surgery not resolved before baseline PET scanning

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-02-2016
Enrollment:	22
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	18F-FDHT
Generic name:	16β-[18F]fluoro-5α-dihydrotestosterone
Product type:	Medicine
Brand name:	bicalutamide
Generic name:	bicalutamide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	22-09-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	24-12-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-03-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-04-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-09-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-10-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-12-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-11-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-12-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-05-2019
Application type:	Amendment
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
EudraCT	EUCTR2015-001634-17-NL
CCMO	NL53358.042.15