Towards early identification of response to cabazitaxel in patients with metastasized castrate-resistant prostate cancer: potential of 18F-Choline PET-CT

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

Summary

ID

NL-OMON46039

Source
ToetsingOnline

Brief title
CABAZIPET

Condition

- Metastases

Synonym
metastatic castration-resistant prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Cyclotron BV,Sanofi-aventis,Sanofi-Aventis (The Netherlands) en Cyclotron BV

Intervention

Keyword: metastatic castration-resistant prostate cancer

Outcome measures

Primary outcome

The main endpoint is the accuracy (e.g. sensitivity, specificity and predictive

values) of FCH-PET measures to detect clinical response, as defined by PCWG2

criteria after 3 and 6 cycles, respectively.

Secondary outcome

The secondary endpoints of this study are:

- predictive value of changes of

o alternative standardized uptake values

o choline avid tumour volume (volume of lesion, defined using PET-based VOIs)

- impact of lesion selection on predictive value

o single lesion versus multiple lesion approach (according to PERCIST)

- interlesional concordance (heterogeneity) of PET signal changes

- serious adverse events (with reference to CTCAE 4.03 criteria) irrespective

of treatment relationship

- cumulative administered dose of cabazitaxel

Study description

Background summary

Cabazitaxel is a tubulin-binding taxane drug that improves survival of patients with docetaxel-castration-resistant prostate cancer (mCRPC). Unfortunately, cabazitaxel is not effective in all patients and can have serious side effects. Therefore, early identification of responding patients might contribute to rational use of cabazitaxel. However, current methods (PCWG2 criteria) to measure response do not meet this need.
Whole body 18F-fluorocholine positron emission tomography (FCH-PET) may qualify as early biomarker of response: PET visualizes and quantifies the uptake of radiolabeled choline; choline metabolism is typically enhanced in prostate cancer. The whole body feature of PET-CT allows for assessment of overall tumor load as well as of individual metastases. In preclinical work, we validated the use of 18F-choline as a potential response read-out to cabazitaxel. In clinical ground-work, we validated simplified PET quantitative measures for use in standard clinical practice, and defined the repeatability of these FCH-PET measures.

Study objective

The main objective of this study is to assess the predictive value of FCH uptake changes as defined with FCH-PET after one cycle of treatment (vs. baseline) to predict clinical response, as defined by PCWG2 criteria, to treatment of mCRPC with cabazitaxel. Secondary objectives are to assess the predictive value of alternative PET measures, the interlesional concordance and the use of a single-lesion versus a multiple-lesion approach.

Study design

A prospective, observational, non-randomized, multicentre phase II study. A whole-body FCH-PET scan will be performed in 30 patients with mCRPC before and after the first cycle of treatment with cabazitaxel. Clinical response according to PCWG2 criteria will be assessed after 3 and 6 cycles, respectively.

Intervention

FCH-PET-CT will be performed with standard state of the art PET-CT scanners, within 3 weeks before the start of cabazitaxel and within one week prior to the second cycle of cabazitaxel. 200 MBq [18F]-fluorocholine will be injected intravenously, followed by a low-dose CT and a dynamic PET scan of thorax region for 30 minutes. After a micturition break, a whole-body PET scan will be performed for 35 minutes.

Study burden and risks

Based on the guideline by the NFU (Dutch Federation of University Medical Centres) about quality insurance in human research (*Kwaliteitsborging van

mensgebonden onderzoek*) we qualify the risk of participating in this study as *low* (small chance of serious damage). The radiation burden patients receive from additional scanning beyond standard care is deemed acceptable for the chosen population.

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. *18 years of age.
2. Signed informed consent according to ICH-GCP before start of treatment and any study specific procedures
3. ECOG Performance Status 0-2.
4. Histological or cytological confirmation of adenocarcinoma of the prostate.
5. Evidence of locally advanced disease, bone-, visceral and/or lymph node metastases on

bone scan, CT-scan or MRI.
6. Continued androgen deprivation therapy either by orchidectomy or GnRH agonist/antagonist
7. Serum testosterone level < 1.7 nmol/L (<50 ng/mL) within 21 days before treatment start
8. Disease progression occurring during or after completion of docetaxel treatment (+ADT) in hormone-sensitive setting or during or after completion of docetaxel treatment (as 1st line) in castration-resistant setting. Patients should have received adequate exposure to docetaxel, that is, not inferior to a cumulative dose of 225 mg/m². Disease progression to be defined as either (1) radiologic disease progression of osseous disease and/or of measurable lesions according to the Prostate Cancer Working Group 2 (PCWG2) criteria and/or (2) prostate-specific antigen progression according to the PCWG2 criteria and disease-related worsening of pain as judged by the treating physician.
9. Treatment with curative intent is not an option and patient has an indication for cabazitaxel as judged by the medical care provider.

Exclusion criteria

1. Impossibility or unwillingness to take oral drugs
2. Geographical, psychological or other non-medical conditions interfering with follow-up
3. Uncontrolled severe illness or medical condition.
4. Symptomatic CNS metastases or history of psychiatric disorder that would prohibit the understanding and giving of informed consent.
5. Chemotherapy or immunotherapy (other than LHRH analogues) within the last 4 weeks before study inclusion.
6. Prior treatment with cabazitaxel, abiraterone, enzalutamide or radium-223 post-docetaxel
7. History of severe hypersensitivity reaction (*grade 3) to docetaxel
8. History of severe hypersensitivity reaction (*grade 3) to polysorbate 80 containing drugs.
9. Concurrent or planned treatment with strong inhibitors or strong inducers of cytochrome P450 3A4/5 (a one week wash-out period is necessary for patients who are already on these treatments)
10. Patients who have a concurrent yellow fever vaccination
11. Abnormal liver functions consisting of any of the following (within 21 days before start of treatment): Total bilirubin > 1 x ULN (except for patients with documented Gilbert*s disease); Alanine aminotransferase (ALAT/SGPT) and/or aspartate aminotransferase (ASAT/ALAT) > 1.5 x ULN
12. Abnormal hematological blood counts consisting of any of the following (within 21 days before start of treatment): Absolute neutrophil count < 1.5 x 109/L; Platelets < 100 x 109/L; Hemoglobin < 6.2 mmol/L (< 10.0 g/dL).

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):	08-09-2017
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]-Fluoromethylcholine
Generic name:	[18F]-Fluoromethylcholine

Ethics review

Approved WMO Date:	30-03-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-06-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-05-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-05-2017

Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2015-004937-29-NL
CCMO	NL55621.029.16