Evaluation of 18F-FDHT PET/CT as a predictor of response in patients with metastasized castration-resistant prostate cancer to be treated with enzalutamide.

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Primary objective: to explore 18F-FDHT PET/CT as a predictor of response in patients with metastasized CRPC to be treated with enzalutamide. Secondary objective: to explore 18F-FDHT PET/CT as a predictor of clinical survival endpoints in patients...

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

Summary

ID

NL-OMON41464

Source
ToetsingOnline

Brief title
FuTuRe

Condition

- Metastases

Synonym
Prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Astellas Pharma;Dionex Benelux ;IQ Therapeutic;NovioGendix Research ;Philips Electronics Nederland

Intervention

Keyword: 18F-FDHT, Castration-resistant prostate cancer, Enzalutamide, Metastases

Outcome measures

Primary outcome

Primary end points:

• Measurements at baseline: SUVmax per lesion, SUVmean per lesion and SUVmaxavg per scan.

• Measurements after 4 weeks of treatment (study week 5): SUVmax per lesion, SUVmean per lesion and SUVmaxavg per scan.

• Delta: the difference between SUVmaxavg, SUVmax per lesion and SUVmean per lesion after 4 weeks of treatment (study week 5)) and SUVmaxavg, SUVmax per lesion and SUVmean per lesion at baseline (study week 1).

Response is defined as not progressive. Progressive according to Prostate Cancer Clinical Trials Working Group3:

- For patients with PSA declines at week 13, PSA progression is defined as >= 25% and an absolute increase of >= 2 ng/ml above the nadir (lowest PSA level after treatment) , which is confirmed by a second value 3 or more weeks later (i.e. a confirmed rising trend).

-For patients with no PSA decline at week 13, PSA progression is defined as >=

25% increase and an absolute increase of >= 2 ng/ml above baseline PSA.

Secondary outcome

Secondary end points:

• Time of start of enzalutamide to initiation of radiation therapy (including external beam radiation therapy or systemic radionuclides e.g. Samarium or Strontium).
• Time of start of enzalutamide to first skeletal-related event (defined as pathological fracture, spinal cord compression, bone pain requiring palliative radiotherapy and orthopedic surgery).
• Time of start of enzalutamide to initiation of cytotoxic chemotherapy or CYP-17 inhibitor (abiraterone).
• Overall survival (defined as the time of start of enzalutamide to date of death from prostate cancer and death from other cause).

Study description

Background summary

Worldwide prostate cancer is the second most frequently diagnosed cancer in men. While localized prostate cancer can be treated with curative intent, metastasized prostate cancer has palliative treatment options only. Endocrine deprivation therapy is the mainstay of treatment for patients with metastasized prostate cancer. In the end, prostate cancer progresses in the majority of patients because of progressive tumor growth despite endocrine deprivation therapy: castration-resistant prostate cancer (CRPC). As CRPC progresses, approximately 90% of patients will develop bone metastases, in contrast to lymph node metastases which develop in 20% to 25% of patients. The determination of response to treatment in patients with CRPC is predominantly plagued by the presence of non-measurable bone metastases. Furthermore, current response monitoring of lymph node metastases has several drawbacks. Positron

Emission Tomography (PET) is emerging as a promising imaging modality to evaluate treatment options and predict therapeutic response timely, objectively and quantitatively. 16β-[18F]-fluoro-5α-dihydrotestosterone (18F-FDHT) images the androgen receptor with high binding affinity and selectivity. It is expected that 18F-FDHTPET/CT can give an indication of success or failure early in the treatment course as part of clinical management or within the context of clinical trials. Timely response management may adjust the duration of individual treatment according to its success.

Study objective

Primary objective: to explore 18F-FDHT PET/CT as a predictor of response in patients with metastasized CRPC to be treated with enzalutamide.

Secondary objective: to explore 18F-FDHT PET/CT as a predictor of clinical survival endpoints in patients with metastasized CRPC to be treated with enzalutamide.

Tertiary objective is to collect biopsies of prostate cancer bone and/or lymph node metastases, blood and urine specimens for future research.

Study design

18F-FDHTPET/CT scans will be performed at baseline and after 4 weeks of enzalutamide treatment (study week 5). Response will be determined after 12 weeks of treatment (study week 13) according to Prostate Cancer Clinical Trials Working Group. Clinical survival endpoints will be collected up to 5 years after inclusion. Patients need to sign an additional informed consent for biorepository. Patients can participate in the current study without participation in biorepository. Biopsies of prostate cancer bone and/or lymph node metastases, blood (excluding Circulating Tumor Cells) and urine will be collected at baseline and after 12 weeks of enzalutamide treatment (study week 13). Blood for CTC will be collected at baseline, after 4 weeks of enzalutamide treatment (study week 5) and after 12 weeks of treatment (study week 13).

Intervention

Ezalutamide 160 mg/day.

Study burden and risks

Burden and risks:
- Study visits: frequency is dependent on the duration of enzalutamide treatment.
- Venepucture: minimally invasive procedure. Known risks are: infection and hematoma, frequency is dependent on the duration of enzalutamide treatment.

- Brief Pain Inventory: questionnaire, takes about 10 minutes, once.
- MUGA scan or echocardiogram: echocardiogram: no risks. MUGA scan: an indwelling intravenous catheter needs to be placed which is a minimally invasive procedure; risks are infection and hematoma. Radiation burden is around 3.5 mSv. One of these investigations need to be performed in case of NYHA class III or IV, once.
- Vital signs (pulse rate and blood pressure will be recorded by automatic device and temperature by ear monitor): no risks, frequency is dependent on the duration of enzalutamide treatment.
- Electrocardiogram: no risks, frequency is dependent on the duration of enzalutamide treatment.
- Physical examination: no risks, frequency is dependent on the duration of enzalutamide treatment.
- Weight and height: no risks, frequency is dependent on the duration of enzalutamide treatment.
- Urine collection by patient: no risks, frequency is dependent on the duration of enzalutamide treatment. A digital rectal examination will be performed immediately prior to the collection of urine: no risks (only in case of biorepository): no risks.
- Placement of an indwelling intravenous catheter (18F-FDHT PET/CT scan): minimally invasive procedure. Known risks are: infection and hematoma, twice.
- Placement of a transurethral catheter (18F-FDHT PET/CT scan): minimally invasive procedure. This is a routine procedure on the Department of Urology. Improper catheterization can lead to urethral damage or a urinary tract infection. These complications are however uncommon. Twice.
- 18F-FDHT PET/CT scan: known risks: to date, other than infrequent transient intravenous site discomfort and transient taste disturbances, no adverse events have been noted in clinical 18F-FDHT PET studies. Total 18F-FDHT PET/CT radiation burden is 5.5 mSv. Furthermore the patient has to lay still on his back for 30 minutes.Twice.
- US or CT guided biopsy: minimally invasive procedure and minimal risks like infection and hematoma. Pain will be minimal due to use of local anesthesia. US guided biopsy is only available for lymph node metastases. CT will give radiation burden of approximately 3 mSv. Twice. Only in case of participation in biorepository.
- Enzalutamide: at a daily dose of 160 mg the following treatment-emergent adverse events were reported at a 5% or greater in the integrated safety population with >= 2% absolute increase in indicence over the placebo group of CRPC2: fatigue, arthralgia, diarrhea, hot flush, peripheral edema, musculoskeletal pain, headache, muscular weakness, insomnia, hematuria, hypertension and pollakiuria. Other treatment-emergent adverse events reported in fewer than 5% of patients, but that may be associated with enzalutamide treatment include: falls, nonpathologic fracture, dry skin, puritus, cognitive effects and hallucination.

Benefit:
- Results of phase 1 and 2 clinical trials reported that enzalutamide has

significant antitumor
activity (including decreases in PSA, responses in soft tissue, stabilized bone disease and conversion from unfavorable to favorable circulating tumor cell counts) in men with chemotherapy-naïve and chemotherapy-treated CRPC.
- The determination of response to treatment in patients with CRPC is predominantly plagued by the presence of non-measurable bone metastases. Furthermore, current response monitoring of lymph node metastases has several drawbacks. It is important that accurate methods are available to monitor CRPC treatment response, since demands on health care resources are great.18F-FDHT PET/CT can be a promising imaging modality to evaluate treatment options and therapeutic response timely, objectively and quantitatively. It is expected that 18F-FDHT PET/CT can give an indication of success or failure early in the treatment course as part of clinical management or within the context of clinical trials. Timely response management may adjust the duration of individual treatment according to its success.
- Prostate cancer bone and lymph node metastases are seldom available for experiments. Biopsy material, blood and urine collected in the current trial will be stored in the PCMM biobank for future experiments.

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. Age 50 or older.
2. Histologically or cytologically confirmed adenocarcinoma of the prostate without neuroendocrine differentiation or small cell features.
3. Ongoing androgen deprivation therapy with a gonadotropin-releasing hormone analogue or bilateral orchidectomy.
4. Progressive disease despite androgen deprivation therapy as defined by rising PSA levels or progressive soft tissue or bone disease.
5. Metastatic disease documented by bone lesions on bone scan or by measurable soft tissue disease by CT
6. No prior cytotoxic chemotherapy for prostate cancer.
7. Asymptomatic or mildly symptomatic from prostate cancer
8. Written informed consent

Exclusion criteria

1. Severe concurrent disease, infection, or co-morbidity that, in the judgment of the investigator, would make the patient inappropriate for enrollment.
2. Known or suspected brain metastasis or active leptomeningeal disease.
3. History of another malignancy within the previous 5 years other than curatively treated non-melanomatous skin cancer.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-11-2014
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	18F-FDHT
Generic name:	16β-[18F]-fluoro-5&alfa;-dihydrotestosterone
Product type:	Medicine
Brand name:	enzalutamide
Generic name:	enzalutamide

Ethics review

Approved WMO Date:	18-06-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-02-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-07-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-02-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-07-2015

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-10-2015
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
Other	4086
EudraCT	EUCTR2012-005431-86-NL
CCMO	NL42842.042.13