# A Randomized, Open Label, Multicenter Study of Cabazitaxel Versus an Androgen Receptor (AR; targeted Agent (Abiraterone or Enzalutamide) in mCRPC Patients Previously Treated with Docetaxel and Who Rapidly Failed a Prior AR-targeted Agent (CARD)

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The aim of this phase IVI, randomized, open-label study is to compare the efficacy of cabazitaxel versus an AR targeted agent, in patients previously treated with docetaxel and likely to have primary resistance to AR targeted agents.

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Renal and urinary tract neoplasms malignant and unspecified |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON47271

**Source**
ToetsingOnline

**Brief title**
CARD

### Condition

- Renal and urinary tract neoplasms malignant and unspecified

**Synonym**
Prostate cancer

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Sanofi-aventis
**Source(s) of monetary or material Support:** sponsor/opdrachtgever

## Intervention

**Keyword:** AR-targeted agent, Open-label, Phase IV, prostate cancer

## Outcome measures

### Primary outcome

Radiographic Progression-Free Survival (rPFS) defined as the time from

randomization to the occurrence of one of the following:

* Radiological tumor progression using RECIST 1.1

* Progression of bone lesions using PCWG2 criteria

* Death due to any cause

### Secondary outcome

* PSA response

* Time to PSA progression (TTPP)

* Progression-free survival

* Objective tumor response in patients with measurable disease (RECIST 1.1)

* Duration of tumor response

* Pain intensity palliation

* Time to pain progression

* SSE rate, occurrence of SSE (by clinical evaluation)

* Overal Survival

* Health status/utility(EQ-5D-5L) and according to FACT-P(HRQOL)

* To evaluate the correlation of a signature of resistance to AR-targeted

agents with clinical outcome

via the analysis of circulating tumor cell (CTC) phenotypes.

# Study description

### Background summary

Prostate cancer is the most frequently diagnosed cancer in men, and represents the third cause of male cancer-related death, after lung and colorectal cancers, in Europe .
Treatment of advanced prostate cancer is palliative. Androgen ablation remains the mainstay of treatment, producing a rapid decrease in bone pain, metastases, and prostate-specific antigen (PSA) levels. Nevertheless, in virtually all patients, the tumor becomes resistant to castration within a median of 18 months after castration .
Until 2010, chemotherapy with docetaxel associated with daily prednisone was the unique treatment option having demonstrated a survival benefit in mCRPC, based on results of two phase III trials which included around 2000 patients . Docetaxel every 3 weeks reduced by 24% the risk of death compared to the active comparator mitoxantrone plus prednisone, with a concomitant improvement of pain and quality of life.

Since 2010, the medical management of mCRPC has changed dramatically with five new agents (cabazitaxel, abiraterone, enzalutamide, radium 223, sipuleucel T) having demonstrated a survival benefit in mCRPC patients. The challenge for physicians is now to integrate this broad armamentarium rationally in daily practice and appropriately tailor therapy to optimize treatment outcomes.

### Study objective

The aim of this phase IVI, randomized, open-label study is to compare the efficacy of cabazitaxel versus an AR targeted agent, in patients previously treated with docetaxel and likely to have primary resistance to AR targeted agents.

### Study design

This is a prospective, multicenter, multinational, randomized, open label phase IV study, comparing the efficacy of cabazitaxel at 25 mg/m² plus prednisone (Arm A) versus either enzalutamide at 160 mg once daily or abiraterone acetate at 1000 mg once daily plus prednisone (Arm B) in primary resistant prostate cancer patients.

**Intervention**

The patients will receive one of these three interventions:
- cabazitaxel 25 mg/m2 once every three weeks including prednisone
- enzalutamide 160 mg daily
- abiraterone acetate 1000 mg daily and prenisone.

**Study burden and risks**

Risk are related to blood sampling and possiboe side effects of the (administration of) study drug. The burden to the patient will consist of the number of visits to the hospital as part of this trial.

# Contacts

**Public**
Sanofi-aventis

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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) Histologically or cytologically confirmed prostate adenocarcinoma.
2) Metastatic disease.
3) Effective castration with serum testosterone levels lower than 0.5 ng/mL.
4) Progressive disease defined by at least one of the following:
- Progression in measurable disease (Response Evaluation Criteria in Solid Tumors [RECIST] 1.1 criteria).
- Appearance of 2 or more new bone lesions (Prostate Cancer Working Group 2 [PCWG2]).;- Rising PSA (PCWG2).;5) Having received prior docetaxel for at least 3 cycles (before or after an AR-targeted therapy).
6) Having progressive disease (PD) while receiving AR-targeted therapy with abiraterone acetate or enzalutamide within 12 months of AR treatment initiation (*12 months).
7) A PSA value of at least 2 ng/mL is required at study entry.
8) Prior AR-targeted therapy (abiraterone acetate or enzalutamide) must be stopped at least 2 weeks before study treatment.
9) Signed informed consent.

## Exclusion criteria

1) Prior chemotherapy other than docetaxel for prostate cancer, except estramustine and except adjuvant/neoadjuvant treatment completed more than 3 years ago.;2) Less than 28 days elapsed from prior treatment with chemotherapy, immunotherapy, radiotherapy, or surgery to the time of randomization.;3) Adverse events (excluding alopecia and those listed in the specific exclusion criteria) from any prior anticancer therapy of Grade >1 (National Cancer Institute Common Terminology Criteria [NCI CTCAE] v4.0) at the time of randomization.;4) Eastern Cooperative Oncology Group performance status (ECOG PS) >2 (ECOG 2 must be related to prostate cancer, not to other comorbidities).;5) Prior malignancy. Adequately treated basal cell or squamous cell skin or superficial (pTis, pTa, and pT1) bladder cancer are allowed, as well as any other cancer for which treatment has been completed *5 years ago and from which the patient has been disease-free for *5 years.;6) Participation in another clinical trial and any concurrent treatment with any investigational drug within 30 days prior to randomization.;7) Acquired immunodeficiency syndrome (AIDS-related illnesses) or known HIV disease requiring antiretroviral treatment.;8) Patients with reproductive potential who do not agree to use an accepted and effective method of contraception during the study treatment period and up to 6 months after the last administered dose. The definition of "effective method of contraception" will be based on the Investigator*s judgment.;9) Known allergies, hypersensitivity or intolerance to prednisone or excipients of

abiraterone acetate, enzalutamide, docetaxel, or polysorbate 80.;10) Known history of mineralo-corticoid excess or deficiency.;11) History of seizure, underlying brain injury with loss of consciousness, transient ischemic attack within the past 12 months, cerebral vascular accident, brain arteriovenous malformation, brain metastases, or the use of concomitant medications that may lower the seizure threshold.;12) Unable to swallow a whole tablet or capsule.;13) Inadequate organ and bone marrow function as evidenced by:;- Hemoglobin <10.0 g/dL;;- Absolute neutrophil count <1.5 × 10^9/L;;- Platelet count <100 × 10^9/L;;- aspartate aminotransferase/serum glutamic oxaloacetic transaminase and/or alanine aminotransferase/serum glutamic pyruvic transaminase >1.5 × the upper limit of normal (ULN);;- Total bilirubin >1.0 × ULN;;- Potassium <3.5 mmol/L;;- Child-Pugh Class C;;14) Contraindications to the use of corticosteroid treatment.;15) Symptomatic peripheral neuropathy Grade >2 (NCI CTCAE v4.0).;16) Uncontrolled severe illness or medical condition including uncontrolled diabetes mellitus, history of cardiovascular disease (uncontrolled hypertension, arterial thrombotic events in the past 6 months, congestive heart failure, severe or unstable angina pectoris, recent myocardial infarction within the last 6 months, or uncontrolled cardiac arrhythmia).;17) Concomitant vaccination with yellow fever vaccine.

# Study design

## Design

| | |
|---|---|
| Study phase: | 4 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 22-08-2016 |
| Enrollment: | 15 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |

| | |
|---|---|
| Brand name: | Jevtana |
| Generic name: | Cabazitaxel |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | XTANDI |
| Generic name: | enzalutamide |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Zytiga |
| Generic name: | Abiraterone-acetate |
| Registration: | Yes - NL intended use |

## Ethics review

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|---|---|
| Approved WMO Date: | 22-06-2015 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 29-10-2015 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 06-01-2016 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 02-03-2016 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 17-03-2016 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO | |

| | |
|---|---|
| Date: | 01-04-2016 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 19-07-2016 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 27-07-2016 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 11-11-2016 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 30-11-2016 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 06-12-2016 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 16-03-2017 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 23-07-2018 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 15-08-2018 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO | |

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|---|---|
| Date: | 07-11-2018 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 19-12-2018 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 15-02-2019 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 02-05-2019 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 08-05-2019 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 16-01-2020 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 22-01-2020 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

# 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 | 2014-004676-29 |
| EudraCT | EUCTR2014-004676-29-NL |
| CCMO | NL53072.091.15 |