Randomised, Double-blind, Placebo-controlled, Multicentre Phase III Study of Olaparib Plus Abiraterone Relative to Placebo Plus Abiraterone as First-line Therapy in Men with Metastatic Castration-resistant Prostate Cancer.

Published: 17-10-2018
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This study has been transitioned to CTIS with ID 2024-511144-86-00 check the CTIS register for the current data. Primary objective: To determine the efficacy of the combination of olaparib and abiraterone vs placebo and abiraterone by assessment of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Prostatic disorders (excl infections and inflammations)
Study type	Interventional

Summary

ID

NL-OMON45999

Source
ToetsingOnline

Brief title
PROpel

Condition

- Prostatic disorders (excl infections and inflammations)

Synonym
metastatic castration resistant prostate cancer, prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: opdrachtgever / sponsor: AstraZeneca

Intervention

Keyword: Metastatic Castration-resistant Prostate Cancer, Olaparib (Lynparza)

Outcome measures

Primary outcome

Primary objective: to determine the efficacy of the combination of olaparib and abiraterone vs placebo and abiraterone by assessment of rPFS (Radiographic progression-free survival) in patients with mCRPC (Metastatic castration-resistant prostate cancer) who have received no prior cytotoxic chemotherapy or NHA (New hormonal agent (abiraterone, enzalutamide)) at mCRPC stage.

outcome: rPFS, defined as the time from randomisation to:

1) radiographic progression, assessed by investigator per RECIST 1.1 (soft tissue) and PCWG-3 criteria (bone), or

2) death from any cause, whichever occurs first.

Secondary outcome

Secondary objectives:

* To determine the efficacy of the combination of olaparib and abiraterone vs placebo and abiraterone as assessed by time to start of first subsequent anticancer therapy or death (TFST) in patients with mCRPC who have received no

prior cytotoxic chemotherapy or NHA at mCRPC stage.

* To determine the efficacy of the combination of olaparib and abiraterone vs placebo and abiraterone as assessed by time to pain progression (TTPP) in patients with mCRPC who have received no prior cytotoxic chemotherapy or NHA at mCRPC stage.

* To determine the efficacy of the combination of olaparib and abiraterone vs placebo and abiraterone by assessment of OS in patients with mCRPC who have received no prior cytotoxic chemotherapy or NHA at mCRPC stage.

* To further evaluate the efficacy of the combination of olaparib and abiraterone vs placebo and abiraterone by assessment of time to opiate use, time to an SSRE (Symptomatic skeletal-related event), CTC (circulating tumour cells) conversion, and PFS2 in patients with mCRPC who have received no prior cytotoxic chemotherapy or NHA at mCRPC stage.

* To assess the effect of the combination of olaparib and abiraterone vs placebo and abiraterone on disease related symptoms and HRQoL using BPI-SF and Functional Assessment of Cancer Therapy (FACT) - Prostate Cancer (FACT-P) questionnaires in patients with mCRPC who have received no prior cytotoxic chemotherapy or NHA at mCRPC stage.

* To evaluate tumour and blood samples from patients with mCRPC who have

received no prior cytotoxic chemotherapy or NHA at mCRPC stage for mutations in

BRCA1, BRCA2, ATM and 12 other HRR genes.

* To determine steady-state exposure to abiraterone and its active metabolite

Δ4-abiraterone in the presence and absence of olaparib.

Study description

Background summary

Prostate cancer is a heterogeneous disease and there is no cure for the patients who reach the metastatic castration resistant stage of the disease. Prostate cancer is the most common cancer in men in the Netherlands.

Patients with metastatic castration-resistant prostate cancer will have a median overall survival around the 3 years when starting early with enzalutamide or abiraterone therapy. The median overall survival within the same healthy patient population is around the 15 years and therefore there is a need for an effective and well tolerated treatment for this patient population.

Olaparib inhibits the protein PARP. PARP is responsible for DNA repair. Cancer arises often from genetic abnormality and when that happens the PARP effectiveness can be increased. Olaparib can prevent the survival of cancer cells by preventing repair of damaged DNA is, causing the cancer cells to die.
This phase Ill study will compare the effectiveness (based on radiographic progression-free survival) of Olaparib in combination with Abiraterone compared with abiraterone alone in patients with metastatic castration-resistant prostate cancer.

The concept for treating mCRPC patients with the combination of olaparib and abiraterone was largely based on the observation that PARP inhibition plus androgen deprivation could significantly reduce the growth of prostate cancer cells independent of HRR status, in both in vitro and in vivo model systems.

To determine the efficacy of the combination of olaparib and abiraterone vs placebo and abiraterone by assessment of rPFS in patients with mCRPC who have

received no previous therapy at mCRPC stage.

Study objective

This study has been transitioned to CTIS with ID 2024-511144-86-00 check the CTIS register for the current data.

Primary objective: To determine the efficacy of the combination of olaparib and abiraterone vs placebo and abiraterone by assessment of rPFS (Radiographic progression-free survival) in patients with mCRPC (Metastatic castration-resistant prostate cancer) who have received no prior cytotoxic chemotherapy or NHA (New hormonal agent (abiraterone, enzalutamide)) at mCRPC stage.

Study design

Phase III, dubbelblinded, randomized study. Randomisation 1:1 to:
- Olaparib (300 mg orally twice daily) and Abiraterone (1000 mg orally with 5 mg prednisone twice daily).
- Placebo (oral, twice daily) + Abiraterone (1000 mg oral with 5 mg prednisone twice daily).

Approximately 720 subjects will receive treatment until progression.

Intervention

Patients receive treatment with Olaparib 300 mg twice daily and abiraterone acetate 1000 mg with 5 mg bid prednisone or
Patients receive treatment with Placebo twice daily and abiraterone acetate 1000 mg with 5 mg bid prednisone.

Study burden and risks

On several days during the study the patient will undergo the following assessments:
Anamnesis (at the screening visit also the medical history), Physical Examination, WHO performance status, Vital signs (bloodpressure, pulse, temperature), weight, bonescan and CT or MRI scan, ECG, Blood and urine assessments, tumor biopsy (if necessary), MUGA/ECHO.

Risk of side effects which may be due to combination of olaparib and abiraterone (and prednisone or prednisolone) seen in previous studies are:
Very common (>10% of the patients) side effects:
nausea, vomiting, constipation, asthenia, loss of appetite, back pain, bone

pain, diarrhea, cough, dyspnea, oedema peripheral, infections, pyrexia, abdominal pain, arthralgia, anaemia, neutropenia.

Other observations:
cardiac events have occurred in this study, with more being observed in the patient group who received both abiraterone and olaparib. However, the numbers of events were very small, and the cause of these events is unclear.
Cardiovascular events have been reported in patients treated with abiraterone alone.

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

- Histologically or cytologically confirmed prostate adenocarcinoma

- Metastatic status defined as at least 1 documented metastatic lesion on either a bone scan or a CT/MRI scan.
- First-line metastatic castration resistant prostate cancer (mCRPC) (treatment naïve at mCRPC stage)
- Ongoing androgen deprivation with gonadotropin-releasing hormone analogue or bilateral orchiectomy, with serum testosterone <50 ng/dL (<2.0 nmol/L) within 28 days before randomisation.

Exclusion criteria

- Known additional malignancy that has had progression or has required active treatment in the last 5 years. Exceptions include basal cell carcinoma of the skin, and squamous cell carcinoma of the skin that has undergone potentially curative therapy
- Patients with myelodysplastic syndrome (MDS)/acute myeloid leukaemia (AML) or with features suggestive of MDS/AML
- Patients with brain metastases
- Clinically significant cardiovascular disease

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-04-2019
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	LYNPARZA
Generic name:	Olaparib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Zytiga
Generic name:	Abiraterone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	17-10-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-03-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-04-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-05-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-06-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-03-2020
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-04-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-09-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-09-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-02-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-02-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-04-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-04-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-06-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-06-2021
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-03-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-04-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-10-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-11-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-11-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-12-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-08-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-09-2023
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
EU-CTR	CTIS2024-511144-86-00
EudraCT	EUCTR2018-002011-10-NL
CCMO	NL67082.091.18