A Phase III Double-Blind, Randomised, Placebo-Controlled Study Assessing the Efficacy and Safety of Capivasertib + Abiraterone Versus Placebo + Abiraterone as Treatment for Patients with De Novo Metastatic Hormone-Sensitive Prostate Cancer (mHSPC) Characterised by PTEN deficiency (CAPItello-281)

Published: 28-05-2020
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This study has been transitioned to CTIS with ID 2023-504998-20-00 check the CTIS register for the current data. - To compare the effect of capivasertib + abiraterone relative to placebo + abiraterone by assessment of radiographic progression-free...

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

Summary

ID

NL-OMON52862

Source
ToetsingOnline

Brief title
CAPItello-281

Condition

- Prostatic disorders (excl infections and inflammations)

Synonym
Metastatic Hormone-Sensitive 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: Abiraterone, Capivasertib, Metastatic Hormone-Sensitive Prostate Cancer, PTEN deficiency

Outcome measures

Primary outcome

- To compare the effect of capivasertib + abiraterone relative to placebo +

abiraterone by assessment of radiographic progression-free survival (rPFS) in

patients with PTEN-deficient mHSPC.

Secondary outcome

- To compare the effect of capivasertib + abiraterone relative to placebo +

abiraterone by assessment of overall survival.

- To compare the effect of capivasertib + abiraterone relative to placebo +

abiraterone by assessment of time to start of first subsequent therapy or death

(TFST).

- To compare the effect of capivasertib + abiraterone relative to placebo +

abiraterone by assessment of symptomatic skeletal event-free survival (SSE-FS).

- To compare the effect of capivasertib + abiraterone relative to placebo +

abiraterone by assessment of time to pain progression (TTPP).

- To compare the effect of capivasertib + abiraterone relative to placebo + abiraterone by assessment of time to PSA progression.
- To compare the effect of capivasertib + abiraterone relative to placebo + abiraterone by assessment of time to castration resistance (TTCR).
- To compare the effect of capivasertib + abiraterone versus placebo + abiraterone on fatigue intensity (based on worst fatigue item), fatigue severity domain and fatigue interference domain as assessed by the Brief Fatigue Inventory (BFI).
- To compare the effect of capivasertib + abiraterone relative to placebo + abiraterone by assessment of overall pain severity and pain interference using the BPI-SF questionnaire.
- To compare the effect of capivasertib + abiraterone versus placebo + abiraterone by assessment of disease-related symptoms and HRQoL using the Functional Assessment of Cancer Therapy - Prostate Cancer (FACT-P) questionnaire.
- To compare the effect of capivasertib + abiraterone relative to placebo + abiraterone by assessment of progression-free survival after next-line treatment (PFS2).
- To evaluate the PK of capivasertib in combination with abiraterone.

Study description

Background summary

There is an important unmet medical need for treatments in the de novo mHSPC setting that are able to delay cancer progression and ultimately, death, particularly in patients whose tumours are characterised by PTEN deficiency. Available nonclinical and clinical evidence suggests that the combined inhibition of serine/threonine specific protein kinase (AKT) and the androgen receptor (AR) axis may improve treatment outcomes in mHSPC. The purpose of this study is to determine the efficacy and safety of the combination of the AKT inhibitor capivasertib and the androgen biosynthesis inhibitor abiraterone combined with a steroid, given on a background of androgen deprivation therapy (ADT) in patients with newly
diagnosed, previously untreated mHSPC and PTEN-deficient tumours.

Study objective

This study has been transitioned to CTIS with ID 2023-504998-20-00 check the CTIS register for the current data.

- To compare the effect of capivasertib + abiraterone relative to placebo + abiraterone by assessment of radiographic progression-free survival PFS) in patients with PTEN-deficient mHSPC.

Study design

Phase III, double-blind, randomized, placebo-controlled multi-center international study

Randomised 1 : 1
- capivesertib in combination with abiraterone (+ prednisone/prednisolone) and background ADT
- placebo in combination with abiraterone (+ prednisone/prednisolone) and background ADT

Stratificaton factors:
- combination of volume of disease (high versus low) and presence of visceral metastasis
- geographic location

Intervention

Capivasertib:
Capivasertib 400 mg twice daily taken in an intermittent weekly dosing schedule (day 1 to 4) together with abiraterone 1000 mg once daily during a 28 day treatment cycle.

Placebo:
Placebo 400 mg twice daily taken in an intermittent weekly dosing schedule (day 1 to 4) together with abiraterone 1000 mg once daily during a 28 day treatment cycle.

Recommended concomitant therapy: prednison/prednisolone 5 mg daily together with ADT (investigator's choice)

Study burden and risks

On several days during the study, patients will undergo the following assessments:

- anamnesis (during pre-screening and screening - medical and surgical history)
- physical examination
- height and weight
- vital signs (blood pressere, heart rate, temperature, respiratory rate)
- ECOG/WHO
- symptomatic skeletal event assessment
- MUGA/ Echocardiogram
- blood and urine assessments
- questionnaires: BPI, analgesic log, BFI, FACT-P, PGIS and EQ-5D-5L
- CT/MRI
- Bonescan
- AE/SAE assessments
- Administration of capivasertib/ Placebo and abiraterone

Contacts

Public
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Scientific
Astra Zeneca

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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Asymptomatic or mildly symptomatic, histologically-confirmed de novo metastatic hormone-sensitive prostate adenocarcinoma without smallcell tumours
- Provide a FFPE tissue block (preferred) or slides. Tissue from bone metastases is not acceptable
- A valid PTEN IHC result indicating PTEN deficiency (centralized testing)
- Metastatic disease documented prior to randomisation by clear evidence of >= 1 bone lesion and/or >= 1 soft tissue lesion accurately assessed at baseline and suitable for repeated assessment with CT and/or MRI.
- Candidate for abiraterone and steroid therapy
- Ongoing ADT with GnRH analogue, or LHRH agonists or antagonist, or bilateral orchiectomy
- Eastern Cooperative Oncology Group (ECOG)/WHO performance status 0 to 1 with no deterioration over the previous 2 weeks and minimum life expectancy of 12 weeks
- Able and willing to swallow and retain oral medication
- 7-day Brief Pain Inventory-Short Form (BPI-SF) and Brief Fatigue Inventory(BFI) questionnaires and the analgesic diary during screening completed

Exclusion criteria

-Prior radical prostatectomy or definitive radiotherapy with a therapeutic intent for prostate
cancer. Palliative radiotherapy is allowed providing any wide field of radiation therapy
(eg, more than one-third of the skeleton) withinis completed more than 4 weeks before the

start of study treatment (capivasertib/placebo).

-Major surgery (excl.placement of vascular access,transurethral resection of prostate,bilateral orchiectomy,internal stents) within 4 wks of start of study treatment
-Brain metastases,or spinal cord compression (unless spinal cord compression is asymptomatic, treated and stable and not requiring steroids for at least 4 wks prior to start of study treatment)
-Past medical history of interstitial lung disease,drug-induced interstitial lung disease,radiation pneumonitis which required steroid treatment,or any evidence of clinically active interstitial lung disease
-Any of the following cardiac criteria:
i.Mean resting corrected QT interval (QTc) >470 msec from 3 consecutive ECGs
ii.Any clinically important abnormalities in rhythm, conduction or morphology of resting ECG
iii.Any factors that increase the risk of QTc prolongation or risk of arrhythmic events such as heart failure,hypokalaemia,potential for torsades de pointes,congenital long QT syndrome,family history of long QT syndrome or unexplained sudden death under 40 years of age,or any concomitant medication known to prolong the QT interval
iv.Clinically significant heart disease as evidenced by myocardial infarction, or arterial thrombotic events in the past 6 months,severe or unstable angina,or NYHA or Class II to IV heart failure or cardiac ejection fraction measurement of <50%
v.Experience of any of the following procedures or conditions in the preceding 6months: coronary artery bypass graft,angioplasty,vascular stent,myocardial infarction,angina pectoris,congestive heart failure NYHA Grade >=2
vi.Uncontrolled hypotension - systolic blood pressure <90 mmHg and/or diastolic blood pressure <50 mmHg
vii.Cardiac ejection fraction outside institutional range of normal or <50% (whichever is higher) as measured by echocardiogram (or multiple-gated acquisition scan if an echocardiogram cannot be performed or is inconclusive)
viii.Uncontrolled hypertension (SBP >=160 mmHg or DBP >=95 mmHg).
-Clinically significant abnormalities of glucose metabolism
-Inadequate bone marrow reserve or organ function
-As judged by the investigator, any evidence of severe or uncontrolled systemic diseases
-Unevaluable for both bone and soft tissue progression as defined by meeting both of the following criteria:
i.a "superscan" of bone scan,and
ii.no soft tissue lesion that can be assessed by RECIST criteria
-Previous allogeneic bone marrow transplant or solid organ transplant
-Known additional malignancy that has had progression or has required active treatment in the last 3 years with exceptions

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):	13-01-2021
Enrollment:	20
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	niet beschikbaar
Generic name:	Capivasertib
Product type:	Medicine
Brand name:	Zytiga
Generic name:	Abiraterone
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	28-05-2020
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-07-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-10-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-11-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-02-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	13-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-02-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-03-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	CTIS2023-504998-20-00
EudraCT	EUCTR2020-000346-33-NL
CCMO	NL73857.056.20
Other	volgt