Pharmacokinetic study of enzalutamide and cabazitaxel combination therapy in metastatic castrate-resistant prostate cancer (mCRPC) patients

Published: 18-12-2014
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To investigate the influence of concomitant enzalutamide on the pharmacokinetics of cabazitaxel.

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

Summary

ID

NL-OMON41753

Source
ToetsingOnline

Brief title
Influence of enzalutamide on cabazitaxel PK

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
prostate cancer, prostate carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,Astellas,zie G2

Intervention

Keyword: Cabazitaxel, Enzalutamide, Interaction, Pharmacokinetics

Outcome measures

Primary outcome

Cabazitaxel pharmacokinetics (AUC)

Secondary outcome

Toxicity

Cabazitaxel pharmacokinetics (the maximum concentration (Cmax), steady-state

volume of distribution (Vss) and half-life (t*)).

Study description

Background summary

Cabazitaxel and enzalutamide are currently registered as standard of care second line treatment for mCRPC. Concomitant administration of both drugs might lead to an increased anti tumor effect. However, this drug combination has never been investigated in humans. Therefore, a drug interaction study has to be performed before the efficacy can be evaluated.

Study objective

To investigate the influence of concomitant enzalutamide on the pharmacokinetics of cabazitaxel.

Study design

Fourteen evaluable patients will be enrolled in this crossover trial. Patients ar their own control, as they will receive cabazitaxel monotherapy during the first cycle and concomitant enzalutamide during the second and third cabazitaxel cycle. Pharmacokinetics will be measured clinically up to 24 hours after cabazitaxel administration and on day 7-9 at the outpatient clinic. Cabazitaxel pharmacokinetics of the first cycle (monotherapy) will be compared to pharmacokinetics of the second and third cycle (with concomitant enzalutamide). After the third cabazitaxel cycle enzalutamide will be discontinued and cabazitaxel administration will continue as per standard of

care.

Intervention

Cabazitaxel 25 mg/m2 three weekly intravenously, conform standard of care
Enzalutamide 160 mg daily from day 7-9 until day 42 van de studie

Study burden and risks

Patients are admitted to the hospital for 24 hours during three consecutive (three weekly) cabazitaxel cycles. During these hospital admission blood withdrawals for pharmacokinetic purposes will be performed, which are accompanied by a neglgible risk of bleeding or infection. Concomitant administration of enzalutamide and cabazitaxel might lead to extra toxicity. However, both drugs have a different spectrum of toxicity and therefore it is not expected toxicity will increase significantly compared to monotherapy. As a consequence of CYP3A4 induction by enzalutamide concentrations of cabazitaxel might decrease temporarily.

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

Age * 18 years
Histological or cytological confirmed diagnosis of mCRPC
ECOG Performance Status * 1
Written informed consent according to ICH-GCP prior to screening evaluations
Indication for cabazitaxel treatmentPatients who are, as per local protocol, eligible for treatment with standard of care cabazitaxel. NB: patients are allowed to have had earlier cabazitaxel cycles
Adequate organ function as defined by:
a.Total bilirubin * 1.5 x ULN (except in case of documented Gilbert*s disease)
b.ASAT * 2.5 x ULN (or * 5 x ULN if liver metastases are present)
c.ALAT * 2.5 x ULN (or * 5 x ULN if liver metastases are present)
d.Serum creatinin * 1.5 x ULN

Exclusion criteria

Evidence of central nervous system disease
History of seizure or any condition predisposing to seizure
Use of concomitant medication predisposing to seizure
Use of (over the counter) medication or (herbal) supplements which can interact with either cabazitaxel or enzalutamide, e.g. by induction or inhibition of CYP3A4, CYP2C9 and CYP2C19 (see appendix B and C)
Unable or unwilling to abstain from grapefruit, grapefruit juice, herbal dietary supplements, and herbal tea during the study
Previous use of enzalutamide during the last 6 weeks prior to cabazitaxel treatment
Contraindications for use of enzalutamide

Study design

Design

Study type:	Interventional
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-04-2015
Enrollment:	18
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

Ethics review

Approved WMO Date:	18-12-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-03-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 28269
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2014-005150-19-NL
CCMO	NL51749.078.14
OMON	NL-OMON28269

Study results

Date completed:	05-10-2016
Actual enrolment:	18