The Effect of Enzalutamide on Oxycodone Metabolism in Men with Prostate Cancer

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To investigate the effect of enzalutamide on the pharmacokinetics (PK) of oxycodone following a single 15 mg oral dose of normal-release oxycodone in men with prostate cancer.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON51266

Source
ToetsingOnline

Brief title
ENZYME

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
Pain in prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Deventer Ziekenhuis
Source(s) of monetary or material Support: Deventer Ziekenhuis

Intervention

Keyword: Enzalutamide, Interaction, Oxycodone, Pharmacokinetics

Outcome measures

Primary outcome

Difference in pharmacokinetics of oxycodone in the presence and absence of enzalutamide, expressed in Cmax and AUC0-t.

Secondary outcome

Differences in pharmacokinetics in the presence and absence of enzalutamide, expressed in:

1. Maximum plasmaconcentration (Cmax) of noroxycodone, oxymorphone and noroxymorphone;

2. Area under the plasma concentration versus time curve from time zero to the time (t) corresponding to the last quantifiable concentration (AUC0-t) of noroxycodone, oxymorphone and noroxymorphone;

3. Area under the concentration-time curve from time zero to infinity with extrapolation of the terminal phase (AUC0-*) of oxycodone and its metabolites noroxycodone, oxymorphone and noroxymorphone;

4. Terminal half-life (t1/2) of oxycodone and its metabolites noroxycodone, oxymorphone and noroxymorphone.

Study description

Background summary

Oxycodone is an opioid receptor agonist that is metabolized mainly in the liver by CYP3A4 and 2D6 enzymes. Enzalutamide is one of the next-generation endocrine agents used in patients with (nonmetastatic and metastatic) CRPC. Because enzalutamide is a strong inducer of CYP3A4, it is expected that enzalutamide will reduce the analgesic effects of oxycodone, which is also metabolised along this pathway. This could have an important impact on patients* pain-related

quality of life and on the effective and safe use of oxycodone and enzalutamide.

Study objective

To investigate the effect of enzalutamide on the pharmacokinetics (PK) of oxycodone following a single 15 mg oral dose of normal-release oxycodone in men with prostate cancer.

Study design

A prospective, open-label, two arm parallel study.

Intervention

Subjects will receive a single oral dose of normal-release oxycodone 15 mg.

Study burden and risks

The subjects will visit the hospital once. During this visit they will receive a single oral dose of normal-release oxycodone 15 mg after which nine blood samples (4 ml each) will be collected at seven different times. Oxycodone is a licensed product with a known mechanism of action and side effects. Because it involves a single dose, the risk is low. Moreover, all subjects will be observed for eight hours after intake of the medication on a nursing ward in the hospital and a physician will be available to supervise.
Subjects are men with prostate cancer who are in general an older population. During this study we are aware of the increased risk of side effects in elderly. The experimental group will include men who already use enzalutamide. The control group will be men with prostate cancer (not treated with enzalutamide) to equalize for multiple factors affecting oxycodone metabolism, among which gender, impaired hepatic and renal function and comedication.

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

- Males aged >= 18 years;
- Diagnosed prostate cancer;
- Treated with enzalutamide 160 mg once daily for 40 days (arm 1)

Exclusion criteria

- a body mass index (BMI) outside the range of 18 to 30 kg/m2;
- known metastases in the liver that would affect drug metabolism;
- Child-Pugh classification B or C that would affect drug metabolism;
- known CYP3A4 or CYP2D6 polymorphisms that would affect drug metabolism (patients with a known CYP3A4 or CYP2D6 polymorphism afterwards will be replaced);
- known moderate-severe renal dysfunction (GFR <60 ml/min/1.73m2) that would affect drug metabolism;
- gastrointestinal disorders that would potentially alter absorption;
- previous gastric bypass or gastric band surgery;
- known allergy, hypersensitivity or intolerance to normal-release oxycodone;
- a history of drug abuse or treatment for abuse;
- dose-reduction or >=5 successive days of treatment interruption of enzalutamide within 40 days prior to the study day (arm 1);
- treatment with enzalutamide within 40 days prior to the study day (arm 2);
- use of oxycodone normal-release within 24 hour prior to oxycodone intake or use of oxycodone extended-release within 2 days prior to oxycodone intake;

- use of other medication that would affect oxycodone metabolism, see section 5.2 and appendix B of the study protocol;
- use of other medication that would affect enzalutamide metabolism, see section 5.2 and appendix B of the study protocol (arm 1).

Study design

Design

Study phase:	4
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):	03-08-2021
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	OxyNorm
Generic name:	Oxycodone
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	14-12-2020

Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	14-01-2021
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	01-06-2021
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	02-06-2021
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)

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
EudraCT	EUCTR2020-005087-66-NL
CCMO	NL75669.075.20

Study results

Date completed:	20-09-2022
Actual enrolment:	27

Summary results

Trial is onging in other countries