Midazolam as a potential CYP3A phenotyping probe for cabazitaxel metabolism.

Published: 01-06-2012
Last updated: 26-04-2024

The primary objective of this study is to investigate whether CYP3A phenotype, as measured with midazolam clearance, correlates with cabazitaxel clearance. Our secondary objective is to investigate whether this CYP3A phenotype outperforms BSA as a...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Metastases
Study type	Interventional

Summary

ID

NL-OMON37899

Source
ToetsingOnline

Brief title
MAILMAN-study

Condition

- Metastases

Synonym
prostate cancer - bone metastases

Research involving
Human

Sponsors and support

Primary sponsor: Meander Medisch Centrum
Source(s) of monetary or material Support: Subsidies

Intervention

Keyword: Cabazitaxel, CYP3A, Phenotype, Prostate cancer

Outcome measures

Primary outcome

Pharmacokinetics of midazolam and cabazitaxel.

Secondary outcome

Does not apply

Study description

Background summary

Cabazitaxel is a novel taxane approved for treatment in men with metastasized hormone refractory prostate cancer (MHRPC). Although its dosing is individualized on body surface area (BSA), variability in cabazitaxel exposure explains variability in toxicity.
Cabazitaxel is mainly metabolized by the cytochrome P450 isoenzyme 3A (CYP3A). In cancer patients, CYP3A activity may vary a 4-fold and it is known that BSA does not account for all variability in clearance. Furthermore, in obese and underweight patients BSA is a poor predictor of clearance.
Midazolam is also metabolized by CYP3A and a commonly used CYP3A phenotyping probe for prediction of clearance of other CYP3A substrates. Therefore, clearance of midazolam might be a good predictor for clearance, and thus exposure, of cabazitaxel. This relationship may guide future cabazitaxel dosing individualization studies based on CYP3A phenotyping to optimize treatment and reduce unwanted toxicity.

Study objective

The primary objective of this study is to investigate whether CYP3A phenotype, as measured with midazolam clearance, correlates with cabazitaxel clearance. Our secondary objective is to investigate whether this CYP3A phenotype outperforms BSA as a predictor of clearance.

Study design

Prospective observational cohort study

Intervention

All men will be administered a single intravenous dose of midazolam (2.5mg) before regular treatment with cabazitaxel. After midazolam and after cabazitaxel administration blood samples will be collected for determination of their pharmacokinetics.

Study burden and risks

The nature and extent of the burden associated with participation are considered to be minimal, since the only extra interventions outside of routine clinical care are administration of midazolam and collection of blood samples. There is no individual benefit to be expected from participation.

Contacts

Public
Meander Medisch Centrum

Utrechtseweg 160
3818 ES Amersfoort
NL
Scientific
Meander Medisch Centrum

Utrechtseweg 160
3818 ES Amersfoort
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Metastasized hormone refractory prostate cancer.
Progression of disease during or after treatment with docetaxel.

Exclusion criteria

Severe dyspnea
Myasthenia Gravis
Sleep apnea syndrome.
Severe hepatic dysfunction
Age 80 years and older

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-01-2013
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Dormicum
Generic name:	Midazolam
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	01-06-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2012-000573-24-NL
CCMO	NL39702.100.12