A pharmacokinetic study of Docetaxel and Prednisone in men with metastatic castration-resistant or hormone-sensitive prostate cancer.

Published: 20-06-2016
Last updated: 14-04-2024

In this study we therefore investigate the influence of prednisone on docetaxel exposure in metastatic prostate cancer patients.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON42925

Source
ToetsingOnline

Brief title
Doc-Pred

Condition

- Reproductive neoplasms male malignant and unspecified

Synonym
metastatic prostate cancer

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

Intervention

Keyword: Docetaxel, mPCa, pharmacokinetics, Prednisone

Outcome measures

Primary outcome

To determine the influence of prednisone use on docetaxel pharmacokinetics compared to docetaxel alone in patients with metastatic castration-resistant prostate cancer (mCRPC) and metastatic hormone-sensitive prostate cancer (mHSPC).

Secondary outcome

* To evaluate the incidence and severity of side-effects of treatment with docetaxel in absence and presence of prednisone.

* Other pharmacokinetic outcomes (i.e. clearance, maximum concentration (Cmax))

Study description

Background summary

Co-administration of prednisone with docetaxel is the standard first-line chemotherapy regimen in men with metastatic castration-resistant prostate cancer (mCRPC). The use of prednisone as component in the regimen, though, has remained controversial. A recent report has shown that patients treated with docetaxel + prednisone experienced less febrile neutropenia compared to patients treated with only docetaxel.This observation lends further evidence that a drug-drug interaction between docetaxel and prednisone may alter the pharmacokinetics (PK) of docetaxel. Docetaxel is mainly metabolized in the liver by the cytochrome P450, (CYP) 3A4 and 3A5 subfamilies of iso-enzymes, and prednisone may impact the activity of this metabolic conversion since it*s known to be a CYP3A4 inducer. Taken together, the possible drug interaction between taxanes and prednisone may be explained by increased taxane clearance induced by prednisone, resulting in lower concentrations of circulating drug, which might ultimately impact drug efficacy and side-effects.

Study objective

In this study we therefore investigate the influence of prednisone on docetaxel exposure in metastatic prostate cancer patients.

Study design

Patients will be randomized in arm A: to receive 3 cycles of docetaxel plus prednisone followed by 3 cycles of docetaxel alone or Arm B: 3 cycles of docetaxel alone followed by 3 cycles of docetaxel plus prednisone. Using this design, each patient serves as his own control. Pharmacokinetic (PK) blood samples from docetaxel cycles (75 mg/m2, IV) without prednisone are compared with PK from the docetaxel cycles with concomitant prednisone (10 mg daily, PO).

Intervention

none

Study burden and risks

Patients will be exposed to docetaxel chemotherapy + prednisone, which is the standard therapy in mCRPC and is currently introduced for hormone-sensitive prostate cancer. Every patient will receive three cycles of docetaxel without prednisone as well. It is hypothesized that more side-effects of neutropenia will occur when docetaxel is given without prednisone, with a higher pharmacokinetic exposure of the cytostatic compound.
The burden for patients participating in this study is a 24-hour hospital admission during two cycles and additional blood samples for PK analyses during their admission (12x4mL blood withdrawals during each hospitalizations, so 96mL in total for the entire study).

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Groene Hilledijk 301
Rotterdam 3075EA
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Groene Hilledijk 301
Rotterdam 3075EA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Histologicallly or cytologically confirmed adenocarcinoma of the prostate without neuro-endocrine differentitation or small cell features.;2. Continued androgen deprivation therapy either by gonadotropin releasing hormone (GnRH) analogues or orchiedectomy;3. Age *18 years;4. Metastatic disease progression;5. ECOG performance status 0-1;6. Written informed consent according to ICH-GCP

Exclusion criteria

1. Impossibility or unwillingness to take oral drugs;2. Serious concurrent illness or medical unstable condition requiring treatment;3. Symptomatic CNS metastases or history of psychiatric disorder that would prohibit the understanding and giving of informed consent;4. Known hypersensitivity to studiemedication;5. Use of medication or dietary supplements known to induce CYP3A;6. Any active systemic or local bacterial, viral, fungal - or yeast infection.;7. Abnormal renal function defined as (within 21 days before randomization);8. Abnormal liver functions consisting of any of the following (within 21 days before randomization):;9. Abnormal hematological blood counts consisting of any of the following (within 21 days before randomization):;10. Geographical, psychological or other non-medical conditions interfering with follow-up

Study design

Design

Study type: Interventional

Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-09-2016
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Prednisone
Generic name:	Prednisone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Taxotere
Generic name:	Docetaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	20-06-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	14-07-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	01-11-2016
Application type:	Amendment
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-001269-10-NL
CCMO	NL58003.078.16