Clinical pharmacokinetics of intravenous docetaxel in patients with castration-resistant prostate cancer and non-castration-resistant prostate cancer

Published: 14-12-2017
Last updated: 04-01-2025

To determine the exposure and clearance of intravenous docetaxel in patients with castration-resistant prostate cancer and non-castration-resistant prostate cancer. All samples will be measured with a validated LC-MS/MS method

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

Summary

ID

NL-OMON44297

Source
ToetsingOnline

Brief title
Pharmacokinetics of intravenous docetaxel

Condition

- Reproductive neoplasms male malignant and unspecified

Synonym
prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Nederlands Kanker Instituut - Antoni van Leeuwenhoek

Intervention

Keyword: CRPC, Docetaxel, nCRPC, Pharmacokinetics

Outcome measures

Primary outcome

To compare the clinical pharmacokinetics, specifically exposure and total plasma clearance, of docetaxel between castration-resistant prostate cancer patients and non-castration-resistant prostate cancer patients.

Secondary outcome

• To measure plasma concentrations of docetaxel metabolites M1, M2, M3 and M4

• To determine metabolite pharmacokinetics

• To determine androgen levels in the predose sample and to explore the correlation between androgen levels and docetaxel pharmacokinetics

• To determine α1-acid glycoprotein levels and the free fraction of docetaxel at timepoints t=1h and t=48h and to explore the correlation between these levels and docetaxel pharmacokinetics

• To establish the effect of functional genetic polymorphisms on the pharmacokinetics of docetaxel (21)

• To compare the pharmacokinetics of docetaxel in patients with prostate cancer (both castration-resistant and non-castration-resistant) with literature docetaxel pharmacokinetics in patients with a different solid tumor type

Study description

Background summary

The pharmacokinetics of docetaxel are characterized by substantial interindividual variability. Altered docetaxel pharmacokinetics are reported in patients with castration-resistant prostate cancer and non-castration-resistant prostate cancer, with a 2-fold higher clearance and 2-fold lower area under the curve (AUC) in castration-resistant patients. Presumably, long-term castrate levels of testosterone or the castration-resistant phase of disease cause an increased elimination of docetaxel. The mechanism behind this remains to be elucidated. However, several explanations for increased clearance are given in literature, such as CYP3A4-induction, P-glycoprotein (P-gp, ABCB1) induction, rOat2 induction and 1α-acid glycoprotein induction.

Study objective

To determine the exposure and clearance of intravenous docetaxel in patients with castration-resistant prostate cancer and non-castration-resistant prostate cancer. All samples will be measured with a validated LC-MS/MS method

Study design

After obtaining informed consent, blood will be drawn for pharmacokinetic analysis after routine administration of docetaxel

Intervention

not applicable

Study burden and risks

Patients participating will be hospitalized for 1 day. Blood sampling for pharmacokinetic research is done at 8 time points. As docetaxel is standard of care treatment for this patient population, no additional risk is expected to be associated with study participation.

Contacts

Public
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
Amsterdam 1066 CX
NL
Scientific
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
Amsterdam 1066 CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Histological or cytological metastatic prostate cancer with an indication for systemic treatment with intravenous docetaxel at the discretion of the physician
Planned to receive first time docetaxel for prostate cancer.
• Group 1: Metastatic castration-resistant prostate cancer with progressive disease defined as biochemical and/or radiological progression according to the Prostate Cancer Working group 3 recommendations. (4) These patients have progressive disease despite long term treatment with hormonal therapy, so they have longterm castrate levels of testosterone. Docetaxel is started after progression on hormonal therapy.
• Group 2: Non-castration-resistant metastatic prostate cancer with an indication for first line docetaxel according to standard clinical care. These patients have metastatic disease at diagnosis and they receive their first systemic treatment as a combined treatment with hormonal therapy and docetaxel. The hormonal therapy is started between 12 and 4 weeks prior to the start of docetaxel. Therefore these patients have castrate levels of testosterone at the start of docetaxel.
2. Considered fit for docetaxel treatment as assessed by the treating physician.
3. Castrate levels of testosterone, defined as <= 50 ng/dL (or <= 0.50 ng/mL or 1.73 nmol/L)
4. Age >= 18 years.
5. Able and willing to give written informed consent.

6. Able and willing to undergo blood sampling for PK and pharmacogenetics analysis.
7. Able and willing to comply with study restrictions and to remain at the study center for the required duration.
8. Adequate organ system function.

Exclusion criteria

not applicable

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	09-01-2018
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	14-12-2017
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	26-07-2018
Application type:	Amendment

Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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
CCMO	NL63555.031.17

Study results

Date completed:	18-01-2021
Results posted:	23-05-2022

First publication
02-04-2022