An open-label cross-over proof of concept study to investigate the intratumoral pharmacokinetics of CriPec® docetaxel versus Taxotere® (the CRITAX study)

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To demonstrate a 25% increase of docetaxel in tumor tissue after intravenous with CriPec® docetaxel compared to Taxotere®. Additionally, systemic PK profile and adverse events will also be evaluated.

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

Summary

ID

NL-OMON47152

Source
ToetsingOnline

Brief title
The CRITAX study

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
cancer malignancy

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Cristal Therapeutics

Intervention

Keyword: CriPec® docetaxel, Intratumoral docetaxel, pharmacokinetics, Taxotere®

Outcome measures

Primary outcome

To show a 25% difference in concentration of docetaxel in tumor tissue after

administration of CriPec® docetaxel compared to Taxotere®.

Secondary outcome

Systemic pharmacokinetics and adverse events:

1. Plasma levels of total and free docetaxel up to 24 hours after dosing and at

the time of biopsy; Cmax, Tmax, AUClast, AUCinf, Thalf, Cl, Vss in relation to

body weight (kg) where applicable.

3. The incidence of Grade 3 or 4 adverse events during cycle 1 and 2 according

to CTCAE, version 4.03.

Docetaxel PK and pathological changes in the skin after treatmet with CriPec®

docetaxel and Taxotere®.

Study description

Background summary

Many conventional chemotherapeutics including docetaxel (Taxotere®) have a

narrow therapeutic index with limitations of drug resistance and lack of selectivity. Additionally, barriers at the tumor site such as abnormal blood supply, abundant tumor stroma and high intratumoral pressure limit tumoral drug penetration, leading to suboptimal therapeutic drug levels. CriPec® docetaxel consists of docetaxel conjugated to a linker agent entrapped in a stabilized CriPec® nanoparticle. CriPec® docetaxel has been designed to accumulate in tumor tissue to a higher extent than native Taxotere® due to the *enhanced permeability and retention* (EPR) effect. Subsequent release of docetaxel from the entrapped particles will allow for an enhanced local anti-tumor effect, whilst docetaxel exposure in non-tumor tissue will remain limited. Preclinical data from mice provided that CriPec® docetaxel (30 mg/kg) had a 20-fold ($P < 0.01$) and 59-fold ($P < 0.001$) higher total docetaxel level as compared to Taxotere® (30 mg/kg) two or 4 days after infusion, respectively. This is the first attempt to provide proof of concept for this in a clinical setting.

Study objective

To demonstrate a 25% increase of docetaxel in tumor tissue after intravenous with CriPec® docetaxel compared to Taxotere®. Additionally, systemic PK profile and adverse events will also be evaluated.

Study design

This is a randomized cross-over study evaluating intratumoral PK of intravenous CriPec® docetaxel compared to generic Taxotere®.

Intervention

Subjects will be randomized in a 1:1 ratio to receive CriPec® docetaxel in cycle 1 and Taxotere® in cycle 2 (Arm A) or Taxotere® in cycle 1 and CriPec® docetaxel in cycle 2 (Arm B). CriPec® docetaxel will be administered at a dose of 75 mg/m2 (4-weekly, Q4W) and Taxotere® also at a dose of 75mg/m2 (3-weekly, Q3W). Tumor biopsies will be taken at 6 different time points (resp. 24, 48, 72, 96, 168 (± 24) or 336 (± 24) hours) after infusion. For each time point 4 patients will be allocated. Additionally punch skin biopsies will obtained at baseline and on day 8 of cycle 1 and 2 for PK analysis of docetaxel in the skin. After completion of cycle 2, a radiographic evaluation will take place and the patients will go off study. Subjects without evidence of disease progression or drug related toxicity can continue treatment with Taxotere® (75mg/m2, Q3W) according to local standard guidelines for Taxotere® treatment until disease progression or unacceptable toxicity occurs.

Study burden and risks

Patients will be exposed to CriPec® docetaxel and Taxotere®. Taxotere® is a registered chemotherapy. It is hypothesized that treatment with CriPec®

docetaxel will result in less side effects and a better antitumor activity. The burden for patients participating in this study includes approximately 2x 24 hours hospital admissions, additional blood withdrawal for PK analyses (30 x 7ml), 8 outpatient clinic visits and two needle biopsy of the tumor and two punch skin biopsies. The number of site visits during cycle 1 and cycle 2 is more than the regular treatment with Taxotere®; participants have 6 additional site visits. The main risks anticipated are: a small bleeding risk after the biopsies, skin toxicity due to CriPec® docetaxel and other known side effects related to Taxotere® for which the patients will carefully be monitored.

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;Patients with advanced, unresectable and/or refractory solid tumors with no

standard therapy options who could benefit from treatment with taxane containing chemotherapy;Signed informed consent;WHO Performance Status 0 or 1;Adequate organ function as defined by:;* Total bilirubine > 1.5 x ULN if no liver metastases (> 2 x ULN in patients with liver metastases). Except in case of documented Gilbert*s disease ;* AST or ALT > 2.5 x ULN if no liver metastases (> 5x ULN in patients with liver metastases);* Creatinine > 1.5 x ULN;Estimated life expectancy of at least 12 weeks;Willing to undergo repeated tumor and skin biopsies

Exclusion criteria

Pregnant or lactating patients;Less than 4 weeks (prior to Cycle 1 Day 1) treatment with another Investigational Product or participation in another investigational interventional study.;Less than 4 weeks since the last anti-cancer therapy prior to Cycle 1 Day 1;Toxicities incurred as a result of previous anti-cancer therapy that have not resolved to * grade 2 except skin toxicity, this should be grade 0 at the base line;Known hypersensitivity to any of the Investigational Product*s excipients or taxanes;Symptomatic brain metastasis ;Patients unable to undergo study procedures

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-04-2017
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	CriPec® docetaxel
Generic name:	Docetaxel anhydrous
Product type:	Medicine
Brand name:	Taxotere®
Generic name:	Docetaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	12-05-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-05-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-11-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-07-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-05-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-05-2018

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2016-001924-70-NL
CCMO	NL57671.056.16