Phase 1 study to evaluate the safety of REducing the prophylactic dose of DEXamethasone around docetaxel infusion in patients with early or advanced breast cancer and prostate cancer.

Published: 16-07-2015
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Primary: To determine the optimal dose/recommended dose (RD) of pre-medication dexamethasone around docetaxel infusion.Secondary: * Does a dose reduction of prophylactic dexamethasone around the docetaxel infusion decrease the body*s metabolic...

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

Summary

ID

NL-OMON45067

Source
ToetsingOnline

Brief title
REDEX

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
cancer, carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: breast cancer, docetaxel, profylactic dexamethasone, prostate cancer

Outcome measures

Primary outcome

Primary:

To determine the optimal dose/RD of prophylactic dexamethasone around docetaxel infusion, dependent of occurrence of fluid retention and hypersensitivity reaction, grade III/IV toxicity according to the National Cancer Institute Common Terminology Criteria for Adverse Events version (NCI CTCAE) v4.03.

Secondary outcome

Secondary:

* To measure metabolic response (glucose, insulin, IGF-1) prophylactic dexamethasone on day 0 before chemotherapy.

* To determine the effect of reducing dexamethasone dose on toxicity of chemotherapy according to NCI CTCAE v4.03.

* Patient*s quality of life (descriptive).

* To determine single nucleotide polymorphisms in glucocorticoid receptor to predict metabolic response (glucose, insulin, IGF-1) and side effects.

Side study:

* To measure the effect of dexamethasone on the pharmacokinetics of docetaxel.

Study description

Background summary

The manufacturer recommends two different regimens of prophylactic dexamethasone to prevent hypersensitivity and fluid retention reactions caused by docetaxel:
a 3-day regime of dexamethasone 8mg twice a day starting the day before chemotherapy for breast cancer and for prostate cancer 3 times 8mg dexamethasone on the day of docetaxel infusion, given the concurrent use of prednisone 2dd5mg.
There is little evidence that supports this high dose regimen used nowadays. There is need to re-evaluate this high dosage of dexamethasone for three main reasons. First, dexamethasone can give side effects such as manifestation of latent diabetes mellitus, immunosuppression, personality changes, irritability, euphoria, or mania and mood swings. Second, dexamethasone is an immune suppressor, which might inhibit chemotherapy-induced apoptosis and compromise the efficacy of chemotherapeutic agents. Third, dexamethasone is a CYP3A4 inducer, which might increase docetaxel clearance.
This study aims to evaluate the feasibility of reducing prophylactic of dexamethasone around docetaxel infusion.

Study objective

Primary:
To determine the optimal dose/recommended dose (RD) of pre-medication dexamethasone around docetaxel infusion.

Secondary:
* Does a dose reduction of prophylactic dexamethasone around the docetaxel infusion decrease the body*s metabolic response (glucose, insulin, IGF-1) to dexamethasone?
* Does a dose reduction of prophylactic dexamethasone around the docetaxel infusion influence chemotherapy induced toxicity?
* Does a dose reduction of prophylactic dexamethasone around the docetaxel increase the quality of Life?
* Are there single nucleotide polymorphisms in the glucocorticoid receptor which can predict metabolic response (glucose, insulin, IGF-1) and side effects?

Side study:

Does dexamethasone influence the pharmacokinetics (PK) of docetaxel?

Study design

Multicenter, open label, non-randomized dose de-escalation study

Intervention

Dose of prophylactic dexamethasone will be reduced as follows:

* EBC and ABC:
STEP 1*: 12 mg dexamethasone per day (8-4mg/day) for 3 days starting 1 day before administration. (n=6)
STEP 2*: 8mg dexamethasone per day (8mg once a day) for 3 days starting 1 day before administration. (n=6)
STEP 3*: day -1: 4 mg, day 0: 8 mg, day 1: 4 mg. (n=6)
STEP 4*: day -1: 0 mg, day 0: 8 mg, day 1: 4 mg. (n=6)
STEP 5*: day -1: 0 mg, day 0: 8 mg, day 1: 0 mg. (n=6)
STEP 6*: day -1: 0 mg, day 0: 4 mg, day 1: 0 mg. (n=6)

* PC:
STEP 1*: 2dd 8 mg at 12 and 1 hr before treatment (n=6)
STEP 2*: 8mg dexamethasone 1 hour before treatment. (n=6)
STEP 3A*: 4mg dexamethasone 1 hour before treatment, with concommitant use of 2dd 5mg prednisone. (n=6)
STEP 3B*: 4mg dexamethasone 1 hour before treatment, without concommitant use of prednisone . (n=6)

*If a grade III/IV toxicity (fluid retention or hypersensitivity reaction) occurs in one of the six patients within one cohort, then three additional patients will be treated at that dose level. If a grade III/IV toxicity (fluid retention or hypersensitivity reaction) occurs in two of the six or two of the nine patients, the previous dose level will be chosen as the RD.

Study burden and risks

The risk for patients that participate in dose levels were dexamethasone is reduced around the docetaxel infusion, is probably slightly increased for experiencing hypersensitivity reaction, fluid retention and nausea and vomiting. However, the risk are acceptable because patients will benefit from reducing the dose of dexamethasone by reducing its side effects as manifestation of latent diabetes mellitus, immunosuppression, personality changes, irritability, euphoria, or mania and mood swings and they might have a better quality of life.

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

Patients with early breast cancer, or advanced breast cancer or prostate cancer patients receiving docetaxel (minimal 3 cycles monotherapy or in a combination regimenl)
* Age *18 years
* WHO performance status 0-2
* Adequate bone marrow function: white blood cells (WBCs) *3.0 x 109/l, neutrophils *1.5 x 109/l, platelets *100 x 109/l
* Adequate liver function: bilirubin *1.5 x upper limit of normal (UNL) range, ALAT and/or ASAT *2.5 x UNL (<5 x UNL in case of liver metastases), Alkaline Phosphatase *5 x UNL
* Adequate renal function: the calculated creatinine clearance should be *50 mL/min
* Survival expectation must be > 3 months
* Written informed consent according to the local Ethics Committee requirements

Exclusion criteria

Known hypersensitivity for docetaxel, paclitaxel or other chemotherapeutic agent or products containing polysorbate 80 or an earlier experience of anaphylaxis for food, insect bites, medication or another foreign substance.
* Existence of edema of the limbs or trunk or elsewhere localized.
* Active second malignancy
* Diabetes Mellitus
* Serious other diseases such as recent myocardial infarction (last 6 months), clinical signs of cardiac failure or clinically significant arrhythmias
* Female patients who are pregnant or breast-feeding
* Medical or psychological condition which in the opinion of the investigator would not permit the patient to complete the study or sign meaningful informed consent

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-04-2016
Enrollment:	90
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO
Date: 16-07-2015

Application type: First submission

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 07-12-2015

Application type: First submission

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 21-03-2016

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 08-06-2016

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 24-04-2017

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 09-05-2017

Application type: Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	20-06-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2015-000718-22-NL
CCMO	NL52595.058.15