Studying the relationship between the CYP3A and CYP2D6 probe dextromethorphan and the pharmacokinetics of tamoxifen.

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Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON24889

Bron
NTR

Verkorte titel
N/A

Aandoening

relationship between the CYP3A and CYP2D6 probe dextromethorphan and the pharmacokinetics of tamoxifen in breast cancer patients who require tamoxifen monotherapy

Ondersteuning

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Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Relationships between dextromethorphan clearance and the clearance of tamoxifen in breast cancer patients.

Toelichting onderzoek

Achtergrond van het onderzoek

In this observational trial we would like to study the possible correlation between the probe-drug dextromethrophan and tamoxifen pharmacokinetics. In case a good correlation is available, this might help in a stepwise development of truly individualizing tamoxifen treatment. Study objectives are relationships between dextromethorphan clearance and the clearance of tamoxifen in breast cancer patients; relationships between other PK-parameters (AUC, Cmax and Tmax); effects of known polymorphisms in CYP2D6 and CYP3A and other relevant drug metabolizing enzymes and transporters on the pahrmacokinetics of tamoxifen and dextromethorphan. In one center (Erasmus Medical Center at Rotterdam, the netherlands), a total of 37 eligable patients, treated with a dose of 20 or 40 mg of tamoxifen, depending on their indication, will be given 30 mg dextromethorphan orally at day 1. Pharmacokinetic sampling will be performed at given time-points (pre, 30 min-24hours, in total 9 sampling time points). For dextromethorphan, blood samples will be processed to plasma and stored until analysis by a validated liquid chromatography tandem mass spectometry method. For tamoxifen, blood samples will be processed to serum and stored until analysis by a validated liquid chromatography tandem mass spectometry method.

Doel van het onderzoek

In this observational trial we would like to study the possible correlation between the probe-drug dextromethrophan and tamoxifen pharmacokinetics. In case a good correlation is available, this might help in a stepwise development of truly individualizing tamoxifen treatment.

Onderzoeksopzet

1. Day -28/-1: informed consent;

2. Day 1: pharmaokinetic sampling (pre, 30 min-24hours in total 9 sampling time points).

Onderzoeksproduct en/of interventie

Observational study with pharmacokinetic sampling.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Histological or cytological confirmed history of breast cancer for which treatment with tamoxifen monotherapy is indicated;

2. Age> or = 18 years;

3. WHO 0 or 1;

4. Adequate renal and hepatic functions;

5. Adequate hematological function;

6. Written informed consent;

7. Use of tamoxifen monotherapy for at least 3 weeks.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Pregnant or lactating patients;

2. Patients with reproductive potential must use a reliable method of contraception;

3. Impossibility to take oral drugs;

4. Serious illness or medical unstable condition requiring treatment;

5. Symptomatic CNS-metastases or history of psychiatric disorder that would prohibit the understanding and giving of ijnformed consent;

6. Unwillingness to abstain form grapefruit (juice), (herbal) dietary supplements, herbals and over the counter medication (except paracetamol and ibuprofen) and other drugs known for to seriously interact with CYP3A and/or ABCB1 and/or ABCG2 during the study period;

7. Use of strong CYP3A and/or P-glycoprotein inhibiting and inducing medication, dietary supplements or other inhibiting compounds.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-06-2009
Aantal proefpersonen:	37
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	31-03-2009
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL1653

Register	ID
NTR-old	NTR1751
Ander register	MEC : 09-YYY
ISRCTN	ISRCTN wordt niet meer aangevraagd

Resultaten

Samenvatting resultaten
de Graan et al. Dextromethorphan as a phenotyping test to predict endoxifen exposure in patients on tamoxifen treatment. J Clin Oncol. 2011;29(24):6240-6