Induction of tamoxifen metabolism.

Gepubliceerd: 24-01-2011 Laatst bijgewerkt: 18-08-2022

In this randomized crossover pharmacokinetic study we will investigate the effects of cytochrome P450 enzyme induction (including CYP3A4, CYP2C and CYP2D6) by rifampicin on the metabolism and plasma pharmacokinetics of tamoxifen and its metabolites...

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON23575

Bron
NTR

Aandoening

Breast cancer
Borstkanker

Ondersteuning

Primaire sponsor: Erasmus Medical Center - Daniel den Hoed Kliniek, afdeling Interne Oncologie
Overige ondersteuning: Erasmus Medical Center - Daniel den Hoed Kliniek, afdeling Interne Oncologie

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The effects of cytochrome P450 enzyme induction (including CYP3A4, CYP2C and CYP2D6) by rifampicin on the metabolism and plasma pharmacokinetics of tamoxifen and its metabolites.

Toelichting onderzoek

Achtergrond van het onderzoek

In this randomized crossover pharmacokinetic study we will investigate the effects of cytochrome P450 enzyme induction (including CYP3A4, CYP2C and CYP2D6) by rifampicin on the metabolism and plasma pharmacokinetics of tamoxifen and its metabolites.

Induction of the expression of these CYP-enzymes will probably lead to an increased metabolism of tamoxifen into its (active) metabolites, including endoxifen. If it appears that endoxifen concentrations are significant higher after induction, there is a possibility created to increase endoxifen concentrations in future patients.

The study will be performed in one center (Erasmus Medical Center, Rotterdam, the Netherlands). Twelve patients who use tamoxifen monotherapy (20 or 40 mg) for at least 4 weeks (to guarantee steady state) will be included in this PK study. Patients will be co-treated with rifampicin during 15 days (1 tablet of 600 mg rifampicin per day). Before and after rifampicin co-administration, pharmacokinetic sampling will be performed during a 24 hour clinical period. Blood samples will be analysed by a validated liquid chromatography tandem mass spectometry method. The differences in pharmacokinetic parameters will be statistically evaluated using a paired Student's t-test.

Doel van het onderzoek

In this randomized crossover pharmacokinetic study we will investigate the effects of cytochrome P450 enzyme induction (including CYP3A4, CYP2C and CYP2D6) by rifampicin on the metabolism and plasma pharmacokinetics of tamoxifen and its metabolites.

Induction of the expression of these CYP-enzymes will probably lead to an increased metabolism of tamoxifen into its (active) metabolites, including endoxifen. If it appears that endoxifen concentrations are significant higher after induction, there is a possibility created to increase endoxifen concentrations in future patients.

Onderzoeksopzet

1. Prior to the study: Informed consent;

2. Day 1-15 (arm-A) / 3-17 (arm-B) co-administration of 600 mg rifampicin;

3. Day 15-16 (arm-A) / 17-18 (arm-B) pharmacokinetic sampling for 24 hours (after co-administration of rifampicin during 15 days);

4. Day 46-47 (arm-A) / 1-2 (arm-B) pharmacokinetic sampling for 24 hours (without rifampicin).

Onderzoeksproduct en/of interventie

1. Co-administration of 600 mg rifampicin during 15 days;

2. Dextromethorphan administration (during both clinical periods);

3. Pharmacokinetic sampling.

Contactpersonen

Publiek

Groene Hilledijk 301
Lisette Binkhorst
Erasmus MC Rotterdam
Daniël den Hoed Cancer Center
Department of Medical Oncology
Room AS-24
Rotterdam 3075 EA
The Netherlands
+31 (0)10 7091937

Wetenschappelijk

Groene Hilledijk 301
Lisette Binkhorst
Erasmus MC Rotterdam
Daniël den Hoed Cancer Center
Department of Medical Oncology
Room AS-24
Rotterdam 3075 EA
The Netherlands
+31 (0)10 7091937

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Histological or cytological confirmed diagnosis of breast cancer, for which treatment with

tamoxifen monotherapy is indicated;

2. Use of tamoxifen monotherapy for at least 4 weeks (to guarantee steady-state) and willing to continue the treatment until the end of the study;

3. Age > 18 years;

4. WHO performance < 1;

5. Adequate renal and hepatic functions;

6. Adequate hematological blood counts;

7. Written informed consent;

8. No radiotherapy or chemotherapy within the last 4 weeks before start;

9. No concurrent (over the counter) medication or (herbal) supplements known to induce or inhibit CYP2D6, CYP2C, CYP3A4 and/or P-glycoprotein;

10. No concurrent medication or supplements which can interact with rifampicin;

11. Abstain from grapefruit, grapefruit juice, herbal dietary supplements, and herbal tea during the study.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Pregnant or lactating patients;

2. Impossibility to take oral drugs;

3. Serious illness or medical unstable condition requiring treatment, symptomatic CNS-metastases or history of psychiatric disorder that would prohibit the understanding and giving of informed consent;

4. Contra-indications for rifampicin and/or dextromethorphan use;

5. Use of medications or dietary supplements known to induce or inhibit CYP2D6, CYP2C, CYP3A4 and/or P-glycoprotein;

6. Unwillingness to abstain from grapefruit (juice), (herbal) dietary supplements, herbals, over-the-counter medication (except for low dose of paracetamol and ibuprofen) and other drugs known to seriously interact with CYP3A during the study period;

7. More than one dose of tamoxifen (20 or 40 mg) per day;

8. Non-compliance.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-02-2011
Aantal proefpersonen:	12
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	24-01-2011
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	NL2584
NTR-old	NTR2709
Ander register	METC Erasmus MC, Rotterdam : 2010-394
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
Binkhorst et al. Individualization of tamoxifen treatment for breast carcinoma. Clin Pharmacol Ther. 2012;92(1):62-7