Observational Study; Midazolam as CYP3A phenotyping probe to investigate the effects of lapatinib on hepatic CYP3A activity.

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Lapatinib inhibits the function of Cytochrome P450 3A isoforms and P glycoprotein.

Ethische beoordeling	Niet van toepassing
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON22273

Bron
Nationaal Trial Register

Verkorte titel
N/A

Aandoening

1. cancer;

2. drug-drug interaction;

3. CYP3A;

4. lapatinib.

Ondersteuning

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Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

CYP3A-activity, as determined by midazolam clearance tests.

Toelichting onderzoek

Achtergrond van het onderzoek

In the here-proposed study, we intend to study the in vivo effects of lapatinib on hepatic CYP3A activity, using midazolam as a probe drug. Patients who will be treated with lapatinib as indicated (not combined with any anti-cancer treatment known to modulate (that is inhibit or induce) drug metabolizing enzymes and drug transporters involved in lapatinib elimination) and who are not using any other concomitant medication/substance known to modulate CYP3A-activity, will be asked to participate. Those patients who consent to participate will undergo three midazolam hydroxylation tests: 1–2 days prior to their first administration of lapatinib and 7–8 and 21–22 days after start of therapy (that is, on days they are normally seen for a routine check-up). Knowledge of the in vivo effects of lapatinib on hepatic CYP3A-activity in humans is of utmost importance and may reduce the risk of unintended adverse effects when other (anti-cancer) drugs that are metabolized by CYP3A are concomitantly used with lapatinib. In addition, knowledge of the in vivo effects of lapatinib on the functional expression of hepatic CYP3A may a priori optimize (future) study-protocols investigating combinations of this drug with CYP3A (anti-cancer) substrates characterized by a small therapeutic window.

Doel van het onderzoek

Lapatinib inhibits the function of Cytochrome P450 3A isoforms and P glycoprotein.

Onderzoeksproduct en/of interventie

Patients who will be treated with lapatinib as indicated will be asked to participate. Those patients who consent will undergo three midazolam hydroxylation tests: 1–2 days prior to

their first administration of lapatinib and 7–8 and 21–22 days after start of therapy. 2.5 mg of midazolam will be injected intravenously over a 15-30-second period. 5 mL blood samples will be collected pre-injection, and at 5 min, 30 min, 1h, 2h, 3h, 4h, 5h, 6h, and 8h post-injection from an intravenous catheter.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Any patient who is going to be treated with lapatinib (1,250–1,500 mg once daily);

2. Age >= 18 years;

3. WHO performance status < 2.4;

4. Adequate renal and hepatic functions, as determined within two weeks before planned start of lapatinib treatment (bilirubin < 1.25xULN; aspartate and alanine transferases (ASAT and ALAT) < 2.5xUNL; alkaline phosphatase (Alk Phos) < 5xULN; serum creatinine £ 1.5xULN);

5.Written informed consent;

6. Complete initial work-up prior to the first midazolam hydroxylation test.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Symptomatic CNS-metastases or a history of a psychiatric disorder that would prohibit the understanding and giving of informed consent;

2. Use of and/or unwillingness to abstain from grapefruit, grapefruit juice, star fruit, dietary supplements, herbal tea, herbals, and over-the-counter medication (except for acetaminophen (paracetamol) and ibuprofen) during the study period, starting 3 weeks before the first midazolam hydroxylation test and ending after the third test;

3. Use of and/or unwillingness to abstain from/absence of adequate alternatives of CYP3A, CYP2C8, CYP2C19, BCRP (ABCG2), and P-glycoprotein (ABCB1) modulating (inducing or inhibiting; see also: http://medicine.iupui.edu/flockhart/table.htm)45 co-medication during the study period, starting 3 weeks before the first midazolam hydroxylation test and ending after the third test;

4. Use of and/or unwillingness to abstain from hypnotics and anxiolytics during the study period, starting 2 weeks before the first midazolam hydroxylation test and ending after the third test;

5. Current and/or recent alcohol- and/or drug (both psycholeptics and psychodysleptics)-abuse;

6. Use of and/or unwillingness to abstain from/absence of adequate alternatives of oxazepam, temazepam and midazolam during the study period, starting 3 weeks before the first midazolam hydroxylation test and ending after the third test.

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-01-2008
Aantal proefpersonen:	15
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

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	NL1031
NTR-old	NTR1064
Ander register	: incomplete
ISRCTN	ISRCTN wordt niet meer aangevraagd

Resultaten