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

No registrations found.

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|---|---|
| **Ethical review** | Not applicable |
| **Status** | Recruiting |
| **Health condition type** | - |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON22273

**Source**
NTR

**Brief title**
N/A

**Health condition**

1. cancer;

2. drug-drug interaction;

3. CYP3A;

4. lapatinib.

### Sponsors and support

**Primary sponsor:** Erasmus MC-Daniel den Hoed
Department of Medical Oncology
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the Netherlands

**Source(s) of monetary or material Support:** Erasmus MC-Daniel den Hoed
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## Intervention

## Outcome measures

### Primary outcome

CYP3A-activity, as determined by midazolam clearance tests.

### Secondary outcome

Auto-inhibition of lapatinib, as determined by lapatinib-levels.

# Study description

### Background summary

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.

### Study objective

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

### Intervention

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.

# Contacts

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# Eligibility criteria

## Inclusion criteria

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.

### Exclusion criteria

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.

## Study design

### Design

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| Study type: | Observational non invasive |
| Intervention model: | Other |
| Masking: | Open (masking not used) |
| Control: | N/A , unknown |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 01-01-2008 |
| Enrollment: | 15 |
| Type: | Anticipated |

## Ethics review

Not applicable
Application type: Not applicable

## 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 |
|---|---|
| NTR-new | NL1031 |
| NTR-old | NTR1064 |
| Other | : incomplete |
| ISRCTN | ISRCTN wordt niet meer aangevraagd |

## Study results