

Oral bioavailability of docetaxel in combination with cyclosporin A and activity of the combination in advance breast cancer

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Registration date 10/11/2010	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 10/11/2010	Condition category Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

N98ODO

Study information

Scientific Title

Oral bioavailability of docetaxel in combination with cyclosporin A and activity of the combination in advance breast cancer: A randomised controlled trial

Acronym

N98ODO

Study objectives

1. The systemic exposure of docetaxel after oral administration of docetaxel in combination with cyclosporin A (CsA) is on average at least 50% of the systemic exposure after intravenous administration of the same dose-equivalent.
2. The combination of a single oral dose of docetaxel and CsA is well tolerated by the patients.
3. Oral docetaxel without CsA results in a low systemic exposure (<5% of a dose normalized i.v. administration)
4. Weekly oral docetaxel + CsA at a dose equivalent of 30-35mg/m² i.v. is active in advanced anthracycline pre-treated breast cancer

Ethics approval required

Old ethics approval format

Ethics approval(s)

The institutional review board (Protocol Toetsingscommissie [PTC]), Dutch Cancer Institute, Antonie von Leeuwenhoek Hospital (NKI-AVL) approved on 4th of November 1998 (ref: EV98330)

Study design

Randomised controlled proof of concept study

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use contact details below to request a patient information sheet

Health condition(s) or problem(s) studied

Cancer, advanced breast cancer

Interventions

The study consist of two parts.

1. Part I is Proof of concept study. It consist of two groups of patients:

1.1. Group I is treated in the course 1 with a single oral dose of docetaxel with CsA and 3 weeks later course 2 and all subsequent courses (6 max) consist of a single agent docetaxel i.v., 3 weekly schedule

1.2. Group II is treated in the course 1 with a single oral dose of docetaxel (no CsA) and 3 weeks later course 2 and all subsequent courses (6 max) consist of a single agent docetaxel i.v., 3 weekly schedule

2. Part II Anti-tumour activity is given weekly oral docetaxel with CsA, (q week 8) to patients with measurable disease according to WHO criteria, after 1 prior anthracycline containing pretreatment regimen for advanced disease.

Safety Assessments are performed during the baseline, every course/weekly and at the end of the treatment - medical history, physical examination, performance status WHO, Hb, Wbc+diff, platelets, chemistry, chest X-ray, tumour evaluation.

PK analyses are determined on the first 2 occasions of drug administration

Efficacy is estimated during the tumour evaluation (CT, X-rays and US) during the baseline and every second course according to WHO criteria.

In amendment 2 the mass balance part of the study has been added. Three evaluable patients who are enrolled in the part II study were asked to collect their urine and faeces up to 48 hours which will be further analyzed for docetaxel and metabolites using validated analytical assays.

Intervention Type

Drug

Phase

Phase I/II

Drug/device/biological/vaccine name(s)

Docetaxel, cyclosporin A (CsA)

Primary outcome measure

1. Safety Assessments are performed during the baseline, every course/weekly and at the end of the treatment

1.1. Medical history

1.2. Physical examination

1.3. Performance status WHO

1.4. Haemoglobin (Hb)

1.5. White blood count (WBC) differential platelets

1.6. Chemistry

1.7. Chest X-ray

1.8. Tumour evaluation

2. Pharmacokinetic (PK) analyses are determined on the first 2 occasions of drug administration

Secondary outcome measures

1. Efficacy is estimated during the tumour evaluation (CT, X-rays and US) during the baseline and every second course according to WHO criteria.

2. In amendment 2 the mass balance part of the study has been added. Three evaluable patients who are enrolled in the part II study were asked to collect their urine and faeces up to 48 hours which will be further analyzed for docetaxel and metabolites using validated analytical assays.

Overall study start date

27/10/1998

Completion date

01/06/2001

Eligibility

Key inclusion criteria

Patients must have:

1. Advanced breast cancer, measurable disease according to WHO criteria
2. Treatment with one anthracycline containing regimen, prior adjuvant chemotherapy is allowed
3. > 18 years
4. Life expectancy >3 months
5. No radiotherapy for at least 4 weeks prior to entry on study
6. WBC > $3.0 \times 10^9/l$, platelets > $100 \times 10^9/l$
7. WHO performance status 0-2
8. Written informed consent
9. Previous hormonal therapy, immunotherapy, or local radiotherapy (without compromising the indicator lesions is allowed)
10. No history of other neoplasm, except curatively treated nonmelanoma skin cancer and curatively treated carcinoma in situ of the cervix

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Female

Target number of participants

25

Key exclusion criteria

1. Concomitant use of MDR converting drugs, such as Ca⁺ - entry blockers (verapamil, dihydropyridines), cyclosporine, quinidine, quinine, tamoxifen, megestrol
2. Uncontrolled infectious disease
3. Unresolved (> grade 1) toxicities of previous chemotherapy
4. Impaired renal function (serum creatinine > 160:mol/l, or clearance < 50ml/min)
5. Serum bilirubin > 20:mol/l
6. Serum albumin < 25g/l
7. Bowel obstruction or motility disorders that may influence the reabsorption of drugs
8. Use of H₂-receptors antagonist or proton pump inhibitors
9. Childbearing or no adequate contraception
10. Neurologic disease that may render a patient at increased risk for peripheral or central

neurotoxicity

11. Symptomatic cerebral or leptomeningeal metastases

12. Unable to give written informed consent

13. Unwilling or unable to undergo blood sampling for pharmacokinetics

14. No prior taxane therapy

Date of first enrolment

27/10/1998

Date of final enrolment

01/06/2001

Locations

Countries of recruitment

Netherlands

Study participating centre

Plesmanlaan 121

Amsterdam

Netherlands

1066CX

Sponsor information

Organisation

The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital (NKI/AVL) (Netherlands)

Sponsor details

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Sponsor type

Research organisation

ROR

<https://ror.org/03xqtf034>

Funder(s)

Funder type

Research organisation

Funder Name

The Netherlands Cancer Institute/ Antoni van Leeuwenhoek Hospital (NKI/ALH) (Netherlands)

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date**Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Not provided at time of registration