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

Submission date 25/08/2010	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 10/11/2010	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 10/11/2010	**Condition category** Cancer	[_] Individual participant data [_] 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

Protocol serial number
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 instiutional 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

Study type(s)
Treatment

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 pretretment 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(s)
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. Pharmakinetic (PK) analyses are determined on the first 2 occasions of drug administration

Key secondary outcome(s))
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.

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 > 3.0x10^9/l, platelets > 100x10^9/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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

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
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Sponsor information

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

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

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration