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Weekly administration of oral docetaxel in combination with ritonavir for the treatment of a variety of tumour types

Submission date 11/11/2010	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 10/01/2011	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 10/01/2011	**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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N07DOW

Study information

Scientific Title
Weekly administration of oral docetaxel in combination with ritonavir for the treatment of a variety of tumour types: an optimal dosing study

Acronym
N07DOW

Study objectives
We aim to determine the optimal dose and formulation of oral docetaxel in combination with ritonavir and investigating if the systemic exposure to docetaxel can also be enhanced by other CYP3A4 inhibitors.

Hypothesis:
30 mg oral docetaxel in combination with 100 mg ritonavir is a safe starting dose.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Local Medical Ethics Committee approved on the 11th of October 2007

Study design
Optimal dosing study

Primary study design
Interventional

Secondary study design
Non 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; various docetaxel sensitive-tumours

Interventions
1. Oral and intravenous administration of docetaxel/paclitaxel and CYP3A4 substrates
2. Blood draw for PK and laboratory analasys
3. Computed tomography (CT) every 2 months

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Docetaxel, ritonavir

Primary outcome measure
To determine the maximum tolerated dose (MTD), dose limiting toxicities (DLT), and optimal dose of docetaxel (ModraDOC001) that can safely be administered to patients with cancer in a weekly schedule.

Secondary outcome measures
1. To determine the haematologic and non-haematologic toxicity
2. To preliminary assess anti-tumour activity of docetaxel
3. To determine the effect of ritonavir on the clearance of docetaxel
4. To estimate the apparent oral bioavailability of docetaxel in combination with ritonavir
5. To establish the effect of functional genetic polymorphisms, C1236T (for MDR1) and CYP3A4*1B, on the pharmacokinetics and pharmacodynamics of oral docetaxel and ritonavir
6. To determine the effect of a second ritonavir dose 4 hours post-dose
7. To determine the systemic exposure of the new oral docetaxel formulation (ModraDOC001) in combination with ritonavir
8. To determine the systemic exposure to docetaxel after administration of ModraDOC001 alone.
9. To investigate whether the systemic exposure to docetaxel can also be enhanced by other CYP3A4 inhibitors, especially ketoconazole, grapefruit juice and clarithromycin
10. To investigate whether ritonavir improves the apparent bioavailability of paclitaxel
11. To investigate whether the systemic exposure to paclitaxel can also be enhanced by other CYP3A4 inhibitors, especially ketoconazole, and clarithromycin
12. To determine the systemic exposure of the new oral paclitaxel formulation (ModraPAC001) in combination with ritonavir
13. To preliminary investigate the influence of a double dose of ritonavir 200 mg on the pharmacokinetics of oral docetaxel and paclitaxel

Overall study start date
01/10/2007

Completion date
31/12/2010

Eligibility

Key inclusion criteria
1. Histological or cytological proof of cancer
2. Patients for whom no standard therapy of proven benefit exist
3. Patients who might benefit from treatment with docetaxel, e.g. advanced breast, gastric, oesophagus, bladder, ovarian cancer and non-small cell lung cancer, head and neck cancers, prostate cancer and carcinoma of unknown primary site

4. Aged greater than or equal to 18 years
5. Able and willing to give written informed consent
6. Able and willing to undergo blood sampling for pharmacokinetics
7. Life expectancy greater than or equal to 3 months allowing adequate follow up of toxicity evaluation and anti-tumour activity
8. Minimal acceptable safety laboratory values
8.1. Absolute neutrophil count (ANC) of greater than or equal to 1.5 x 10^9/L
8.2. Platelet count of greater than or equal to 100 x 10^9/L
8.3. Hepatic function as defined by serum bilirubin less than or equal to 1.5 x upper limit of normal (ULN), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) less than or equal to 2.5 x ULN
8.4. Renal function as defined by serum creatinine less than or equal to 1.5 x ULN or creatinine clearance greater than or equal to 50 ml/min (by Cockcroft-Gault formula)
9. World Health Organisation (WHO) performance status of less than or equal to 2
10. No radio- or chemotherapy within the last 4 weeks prior to study entry (palliative limited radiation for pain reduction is allowed)
11. Able and willing to swallow oral medication
12. Arm F: Patients for whom weekly paclitaxel can seriously be considered therapy with palliative intent, with tumour types that reasonably will respond

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Total approx. 78 (Arm A: 30 approx; Arms B-C: 6 per arm; Arms D-L: 4 per arm)

Key exclusion criteria
1. Patients with known alcoholism, drug addiction and/or a history of psychotic disorders that are not suitable for adequate follow up
2. Women who are pregnant or breast feeding
3. Both men and women who do not agree to use a reliable contraceptive method throughout the study
4. Concomitant use of MDR and CYP3A modulating drugs such as Ca+ entry blockers (verapamil, dihydropyridines), cyclosporine, quinidine, quinine, tamoxifen, megestrol and grapefruit juice, concomitant use of human immunodeficiency virus (HIV) medications; other protease inhibitors, (non) nucleoside analoga, or St. Johns wort
5. Uncontrolled infectious disease or known HIV-1 or HIV-2 type patients
6. Unresolved (greater than grade 1) toxicities of previous chemotherapy
7. Bowel obstructions or motility disorders that may influence the resorption of drugs
8. Chronic use of H2-receptor antagonists or proton pump inhibitors
9. Neurologic disease that may render a patient at increased risk for peripheral or central neurotoxicity

10. Symptomatic cerebral or leptomeningeal metastases
11. Acid neutralizing medicines (e.g. aluminium hydroxide), should not be administered for at least 2 hours prior to and after the intake of ketoconazol (Arm D)

Date of first enrolment
01/10/2007

Date of final enrolment
31/12/2010

Locations

Countries of recruitment
Netherlands

Study participating centre
Plesmanlaan 121
Amsterdam
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1066CX

Sponsor information

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

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Sponsor type
Hospital/treatment centre

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