

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

Protocol serial number
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

Study type(s)

Treatment

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 analysis
3. Computed tomography (CT) every 2 months

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Docetaxel, ritonavir

Primary outcome(s)

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.

Key secondary outcome(s)

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

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 $1.5 \times 10^9/L$
 - 8.2. Platelet count of greater than or equal to $100 \times 10^9/L$
 - 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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

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 analogs, 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
Netherlands
1066CX

Sponsor information

Organisation

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