Interaction study of Docetaxel + Tolbutamide and Milk Thistle.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27803

Source
Nationaal Trial Register

Health condition

Pharmacokinetic herb-drug interaction, cancer, docetaxel, milk thistle, tolbutamide

Dutch: farmacokinetische interacties, kanker, docetaxel, mariadistel, tolbutamide

Sponsors and support

Primary sponsor: The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL)
Source(s) of monetary or material Support: Dutch Cancer Society (KWF Kankerbestrijding)

Intervention

Outcome measures

Primary outcome

Pharmacokinetic parameters of docetaxel and tolbutamide on day 1 and 22: AUC, Cmax, t1/2.

Secondary outcome

Safety parameters: (serious)adverse events.

Study description

Background summary

The use of complementary and alternative medicines (CAM) by cancer patients has increased during the last years and we
hypothesize that interactions between CAM and anticancer drugs can explain unexpected clinical toxicities and undertreatment of chemotherapy in cancer patients.

A CAM which is often used by cancer patients is milk thistle. In vitro assays have shown that milk thistle inhibits the activity of the hepatic enzymes CYP2C9 and CYP3A4. Thus, concomitant use of milk thistle could lead to significant interactions with (anticancer) drugs metabolized by these enzymes. In the present study the well-studied CYP2C9 probe drug tolbutamide has been selected to assess the influence of milk thistle on CYP2C9 activity. Docetaxel, which is mainly metabolized by CYP3A4, has been chosen to investigate the effect of milk thistle on CYP3A4 activity.

Inhibition of CYP2C9 and CYP3A4 by milk thistle is expected to increase plasma levels of tolbutamide and docetaxel.

Until now, no studies have been performed to examine the pharmacokinetics of docetaxel and tolbutamide with coadministration of milk thistle. To investigate whether the inhibition of CYP2C9 and CYP3A4 by milk thistle demonstrated in vitro, is of clinical importance, it is essential to perform this pharmacokinetic interaction study.

Study objective

Inhibition of CYP2C9 and CYP3A4 by milk thistle is expected to increase plasma levels of tolbutamide and docetaxel.

Study design

Day 1 and 22: PK sampling docetaxel and tolbutamide.

End of treatment assessment on day 42.

Intervention

Day 1 and day 22: 135 mg docetaxel (IV) + 250 mg tolbutamide (PO).

Cohort A: Three times daily one 180 mg capsule of milk thistle on day 0, 1, 2 and 3;

Cohort B: Three times daily one 180 mg capsule of milk thistle on day 21, 22, 23 and 24.

Contacts

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Eligibility criteria

Inclusion criteria

1. Patients for whom treatment with docetaxel is considered to be
of therapeutic benefit, e.g. advanced breast, gastric, esophagus,
bladder, ovarian cancer and non-small cell lung cancer, head and neck cancer and prostate cancer;

2. Histological or cytological proof of cancer;

3. Age ≥ 18 years;

4. WHO performance status of 0, 1 or 2;

5. Patient is able and willing to give written informed consent;

6. Patient is able and willing to swallow and retain oral medication;

7. Patient is able and willing to undergo blood sampling for pharmacokinetics;

8. Patient is willing to comply to the protocol and to follow dietary restrictions;

9. Life expectancy ≥ 3 months allowing adequate follow up of toxicity evaluation and antitumor activity;

10. Minimal acceptable safety laboratory values:

A. ANC of ≥ 1.5 x 10^9 /L;

B. Platelet count of ≥ 100 x 10^9 /L;

C. Hepatic function as defined by serum bilirubin ≤ 1.5 x ULN, ALAT and ASAT ≤ 2.5 x ULN;

D. Renal function as defined by serum creatinine ≤ 1.5 x ULN or creatinine clearance ≥ 50 ml/min (by
Cockcroft-Gault formula).

11. No radio- or chemotherapy within the last 4 weeks prior to study entry, except for pain palliation.

Exclusion criteria

1. Any treatment with investigation drugs within 30 days before the start of the study;

2. Patients with known alcoholism, drug addiction and/or a psychiatric or physiological condition which in the opinion of the investigator would impair study compliance;

3. Women who are pregnant or breast feeding;

4. Unreliable contraceptive methods. Both men and women enrolled in this trial must agree to use a reliable contraceptive
method throughout the study (adequate contraceptive methods are: condom, contraceptive pill (female partner), abstinence from sexual intercourse, sterilisation of man or woman);

5. Legal incapacity;

6. Concomitant use of MDR, CYP2C9 and CYP3A modulating drugs such as amiodaron, fluconazole, ketoconazole,
clarithromycin, rifampicin, Ca+-entry blockers (verapamil, dihydropyridines), cyclosporine, quinidine, quinine,
tamoxifen, megestrol and grapefruit juice, concomitant use of HIV medications; other protease inhibitors, (non) nucleoside analogs, or St. John's wort;

7. Type I and II diabetes mellitus patients;

8. Uncontrolled infectious disease or known HIV-1 or HIV-2 type patients;

9. Unresolved (>grade 1) toxicities of previous chemotherapy;

10. Bowel obstruction or motility disorders that may influence the absorption of drugs;

11. Chronic use of H2-receptor antagonists or proton pump inhibitors;

12. Neurologic disease that may render a patient at increased risk for peripheral or central neurotoxicity;

13. Symptomatic cerebral or leptomeningeal metastases;

14. Use of herbal supplements, especially milk thistle, within 6 weeks prior to study treatment.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-03-2012
Enrollment:	10
Type:	Anticipated

Ethics review

Positive opinion

Date:	13-09-2012
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 39305
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL3459
NTR-old	NTR3611
CCMO	NL34285.031.10
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON39305

Study results

Summary results
N/A