Effects of omeprazole on the pharmacokinetics of irinotecan in cancer patients.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28883

Source
NTR

Brief title
OMEPIRI

Health condition

Cancer.

Sponsors and support

Primary sponsor: Erasmus MC - Afdeling Interne Oncologie
Source(s) of monetary or material Support: fund=initiator=sponsor

Intervention

Outcome measures

Primary outcome

Plasma pharmacokinetics (PK) of irinotecan and its metabolites.

Secondary outcome

1. Side effects, especially neutropenia and late-onset diarrhea;

2. Hepatic CYP3A activity, as determined by the intravenous midazolam hydroxylation test.

Study description

Background summary

This single center, open-label crossover study intends to investigate the possible pharmacokinetic interaction of omeprazole and irinotecan. The study will be performed at the Erasmus MC, location Daniel den Hoed Cancer Center. A total of 14 evaluable patients will be treated. Based upon recently conducted retrospective and prospective studies of the pharmacokinetics of irinotecan as a function of BSA (body surface area), which showed that BSA-based dosing does not reduce interpatient variability in irinotecan pharmacokinetics and drug-associated toxicities (Mathijssen, JCO, 2002 & de Jong, CCR, 2004), we will administer a 600 mg flat-fixed dose of irinotecan (3-weekly, 90-minutes i.v.) to all included patients. Patients will be deemed evaluable when treated with two courses of irinotecan; one course without and one course with concomitant use of omeprazole, and complete pharmacokinetic sampling and toxicity assessment has been performed according to this protocol.
All patients will receive their first course of irinotecan without concomitant omeprazole followed by a second course of irinotecan with concomitant use of omeprazole (Losec MUPS) 40 mg QD, starting at day 8 of the first course until the third day of the second course. Both courses of irinotecan will be preceded by a midazolam hydroxylation test, performed on day 0 of both courses.

Study objective

To investigate the influence of omeprazole on the metabolism and plasma pharmacokinetics (PK) of irinotecan and its metabolites in cancer patients.

Study design

N/A

Intervention

In this open-label crossover pharmacokinetic study, we will compare the plasma pharmacokinetics of irinotecan and its metabolites in patients treated with courses of irinotecan with and without concomitant use of omeprazole. Patients will receive irinotecan at 600 mg (90 min. i.v. infusion) without omeprazole during the first treatment cycle. In the second treatment cycle, these patients will be pretreated with 40 mg omeprazole for 14 days, and will then receive the second infusion of irinotecan (600 mg). Omeprazole will be continued until the third day after the second irinotecan infusion.
Both courses of irinotecan will be preceded by a midazolam hydroxylation test, performed on

day -1 of both courses.

Contacts

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Eligibility criteria

Inclusion criteria

1. Histological or cytological confirmed diagnosis of any form of (irresectable and/or metastatic) cancer, which is thought to be sensitive to irinotecan-treatment;

2. Age >= 18 years;

3. WHO performance status <= 1;

4. Adequate hematological functions (ANC > 1.5 x 109/L (ANC between 1.5 and 2.0, must be approved by the study coordinators), platelets > 100 x 1012/L);

5. Adequate renal and hepatic functions (serum creatinin < 1.25xULN, bilirubin < 1.25xULN; ALAT and ASAT < 2.5xULN, in case of liver metastasis < 5xULN; alkaline phosphatase < 5xULN; gamma-GT < 5xULN;

6. Written informed consent;

7. Complete initial work-up within two weeks prior to chemotherapy.

Exclusion criteria

1. Pregnant or lactating patients; patients with reproductive potential must use a reliable method of contraception (excluding oral contraceptives), if required;

2. Serious illness or medical unstable condition requiring treatment, symptomatic CNS-metastases or history of psychiatric disorder that would prohibit the understanding and giving of informed consent;

3. Time between last antitumor treatment and first day of irinotecan therapy less than 4 weeks, provided that the patient has recovered from relevant toxic effects;

4. Radiotherapy within the last 4 weeks before the first course, if more than 20% of the bone marrow area is involved;

5. Major surgery within 4 weeks before the first course (to be evaluated by an MD);

6. Unresolved bowel obstruction or chronic colic disease;

7. Unwillingness to abstain from grapefruit(juice), star fruit (carambola), (herbal) dietary supplements, herbal tea, herbals and over-the-counter medication (except for paracetamol and ibuprofen) during the study period (starting two weeks before the first midazolam hydroxylation test);

8. Unwillingness to change medication, or no adequate alternatives available, in case of (chronic) use of CYP3A and/or P-glycoprotein inhibiting or inducing medication, dietary supplements, or other influencing compounds during the study period (starting two weeks before the first midazolam hydroxylation test);

9. Unwillingness to change medication in case of use of midazolam, temazepam and/or diazepam during the study period (starting two weeks before the first midazolam hydroxylation test);

10. Use of omeprazole or any other proton pump inhibitor during the study period (starting two weeks before the first midazolam hydroxylation test).

Study design

Design

Study type:	Interventional
Intervention model:	Crossover

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-01-2008
Enrollment:	14
Type:	Actual

Ethics review

Positive opinion

Date:	18-01-2008
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
NTR-new	NL1137
NTR-old	NTR1179
Other	METC : METC-2007-380
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results
N/A