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CYP3A4 phenotype-based dosing of irinotecan

Submission date 11/06/2009	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 27/07/2009	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 27/07/2009	**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
MEC04-290

Study information

Scientific Title
A new dosing strategy to lower inter-patient variability of irinotecan pharmacokinetics in cancer patients: a two-centre randomised controlled parallel phase II study

Study objectives
The use of an irinotecan dosing strategy based on a formula derived from the midazolam clearance test, gamma-glutamyl transpeptidase (gamma-GT) and height, should lower inter-patient variability in first course pharmacokinetics in cancer patients, compared to a classic dose-strategy based on body-surface area (BSA).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Erasmus Medical University Centre Ethics Board approved on the 4th August 2005.

Study design
Multicentre randomised controlled parallel phase II 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 the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Cancer

Interventions
1. Single midazolam clearance test (MCT), involving midazolam infusion and pharmacokinetic measurements
2. Regular laboratory testing prior to irinotecan infusion, and weekly outpatients controls
3. Irinotecan infusion (90 minutes intravenously [iv] every three weeks [q3w]) and irinotecan pharmacokinetic measurements during the first course (3 weeks)

For the irinotecan infusion, patients were divided into two groups:
Group A: patients received a dose of irinotecan based on the new formula
Group B: patients received a dose based on classic body surface area (BSA) -based dosing

The course of chemotherapy was given in 90 minutes, once every three weeks. During those 3 weeks extra blood samples for pharmacokinetic analyses were taken and toxicity measures (i.e. neutropenia) were scored. After that one course, there was no follow-up.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Irinotecan

Primary outcome measure
Pharmacokinetics (AUC/clearance) of midazolam, irinotecan and metabolite SN-38, determined by LC-MS-MS and calculated using WinNonlin, measured during the infusion period and for the next 3 weeks

Secondary outcome measures
Toxicity assessment (i.e. leukopenia, neutropenia, neutropenic fever, diarrhoea), measured during the infusion period and for the next 3 weeks

Overall study start date
01/09/2005

Completion date
01/09/2007

Eligibility

Key inclusion criteria
1. Histological or cytological confirmed diagnosis of any form of cancer, which is thought to be sensitive to irinotecan-treatment
2. Aged 18 years or older, either sex
3. World Health Organization (WHO) performance status 0 or 1
4. Adequate haematological functions, as determined 2 weeks before inclusion and within 2 days before start of irinotecan infusion (neutrophil count greater than 2.0 x 10^9/l, platelets greater than 100 x 10^9/L)
5. Adequate renal and hepatic functions, as determined 2 weeks before inclusion and within 2 days before start of irinotecan infusion (bilirubin less than 1.25 x upper limit of normal [ULN]; serum glutamic oxaloacetic transaminase [SGOT]/serum glutamic pyruvate transaminase [SGPT] less than 2.5 x ULN, in case of liver metastasis less than 5 x ULN; serum creatinine less than 1.25 x ULN; alkaline phosphatase [AP] less than 5 x ULN; gammaGT less than 200 U/l)
6. Written informed consent
7. Complete workup within 2 weeks prior to chemotherapy

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex

Both

Target number of participants
40 evaluable patients

Key exclusion criteria
1. Pregnant or lactating patients
2. Other serious illness or medical unstable conditions requiring treatment
3. Symptomatic central nervous system (CNS) metastases
4. History of psychiatric disorder
5. Time between last anti-tumour chemotherapy treatment and first day of irinotecan therapy less than 4 weeks
6. Radiotherapy within 4 weeks before chemotherapy, unless less than 20% of bone marrow area is involved
7. (Recent) radiotherapy at abdomen
8. Major surgery within 4 weeks before study entry
9. Unresolved bowel obstruction or chronic colic disease
10. Use of, and unwillingness to abstain from grapefruit (juice), herbal supplements/tea/over the counter medicines during the study period (starting 3 weeks before the first course). (Chronic) use of CYP3A and Pgp inhibiting/inducing medication, dietary supplements, or other inhibiting compounds.

Date of first enrolment
01/09/2005

Date of final enrolment
01/09/2007

Locations

Countries of recruitment
Netherlands

Study participating centre
Groene Hilledijk 301
Rotterdam
Netherlands
3075 EA

Sponsor information

Organisation
Erasmus Medical Centre (Netherlands)

Sponsor details

Groene Hilledijk 301
Rotterdam
Netherlands
3075EA

Sponsor type
Hospital/treatment centre

Website
http://www.erasmusmc.nl/

ROR
https://ror.org/018906e22

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Pfizer Inc. (Netherlands) - provided medication; no financial support

Funder Name
Erasmus Medical Centre (Netherlands) - Daniel den Hoed Kliniek covered costs for pharmacokinetic measurements

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