Dietary restriction followed by irinotecan chemotherapy

No registrations found.

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

Summary

ID

NL-OMON29351

Source
NTR

Brief title
DIRINO study

Health condition

Dietary restriction
Fasting
Metastatic colorectal carcinoma
Irinotecan

Dieetrestrictie
Vasten
Gemetastaseerd colorectaal carcinoom
Irinotecan

Sponsors and support

Primary sponsor: Erasmus Medical Center
Source(s) of monetary or material Support: Erasmus Medical Center

Intervention

Outcome measures

Primary outcome

Primary objective is to demonstrate a 25% reduction of the active irinotecan metabolite, SN38, in healthy liver tissue (without reducing the intra-tumoral SN38 concentration) in patients with mCRC and other solid tumors as a result of preceding dietary restriction.

Secondary outcome

Secondary objectives are systemic and intratumoral irinotecan pharmacokinetics and toxicity.

Study description

Background summary

Currently, more than half of the metastatic colorectal cancer patients do not benefit (optimally) from intravenously administered irinotecan as second line treatment. In recent preclinical studies in mice we have shown that the anti-tumor effects of irinotecan can be enhanced by fasting before irinotecan treatment. In addition, toxicity may be seriously reduced by fasting. While mice are significantly protected from the side effects of irinotecan chemotherapy after 72 hours of fasting, SN-38 (the active irinotecan metabolite) concentrations in both plasma and liver were significantly lower and intra-tumoral drug concentrations tend to be higher. The DIRINO study is a randomised two-arm cross-over study during which patients with mCRC and other solid tumors will be using a dietary restriction regimen for five days prior to the first or second irinotecan cycle. Primary endpoint is to demonstrate a 25% reduction of the SN-38 concentrations in healthy liver tissue (without reducing the intra-tumoral SN-38 concentration) 24 hours after irinotecan administration with preceding dietary restriction compared to no preceding dietary restriction. Secondary objectives are toxicity, systemic and intra-tumoral irinotecan pharmacokinetics.

Study objective

Short term dietary restriction will lead to lower concentrations of SN-38 in healthy liver tissue (without reducing the intratumoral concentration) and to less toxicity of irinotecan

Study design

First and second cycle of irinotecan treatment.

Intervention

Standard treatment with or without dietary restriction

Contacts

Public
Erasmus MC Cancer Institute - Department of Internal Oncology

F.M. de Man
‘s Gravendijkwal 230

Rotterdam 3015 CE
The Netherlands
Tel: +31 (0)10 7042451
Scientific
Erasmus MC Cancer Institute - Department of Internal Oncology

F.M. de Man
‘s Gravendijkwal 230

Rotterdam 3015 CE
The Netherlands
Tel: +31 (0)10 7042451

Eligibility criteria

Inclusion criteria

• Metastatic colorectal cancer and other solid tumors

• Treatment with irinotecan 600 mg 3-weekly

• Age ≥ 18 years

• BMI:20-30 kg/m2

• WHO performance status 0-1

• Written informed consent

• Adequate renal function, i.e. serum creatinin < 2 x ULN and creatinin clearance > 45 mL/min (calculated with Cockroft-Gault formula)

• Patients with safely accessible liver metastases and healthy liver tissue

• Adequate coagulation status as measured by:

o PT-INR < 1.5

o APTT < 1.5 x ULN

o Hb > 6 mmol/L

 Note: Red blood cell transfusions are allowed to increase the Hb at the discretion of the investigator, but not during blood withdrawal for PK-analysis. Any necessary red blood cell transfusions during the first three cycles of irinotecan will be reported in the article.

o Platelet count > 100 x 109/L

Exclusion criteria

• Previous treatment with irinotecan within the last 6 months

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

• Serious illness or medical unstable condition prohibiting adequate treatment and follow-up.

• History of bleeding disorders (such as hemophilia) or bleeding complications from biopsies, dental procedures or surgeries.

• Patients using any anti-coagulant medication which cannot be safely stopped or counteracted at the time of biopsy: all aspirin derivatives, NSAIDs, coumarines, platelet function inhibitors, heparins (including LMWHs) and oral factor Xa inhibitors.

• Unable or unwilling to stop the use of (over the counter) medication of (herbal) supplements which can interact with irinotecan (e.g. by induction or inhibition of CYP3A4 (see Appendix B))

• Patients using insulin

• Patients with hyperventilation

• Patients unable of unwilling to fill in a food diary

• Patients using oxygen and not able to stop for 30 minutes

• Unable or unwilling to abstain from grapefruit or grapefruit juice during the study

• Bilirubin > 1.5 x ULN, AF > 5x ULN, ASAT > 5x ULN, ALAT >5x ULN

• Uncontrolled hypertension, despite medical treatment

• Cows milk and/or soy allergy and/or lactose intolerance

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:	Recruitment stopped
Start date (anticipated):	11-03-2016
Enrollment:	18
Type:	Actual

IPD sharing statement

Plan to share IPD: No

Plan description
Data can be requested by emailing the investigator

Ethics review

Positive opinion

Date:	04-03-2016
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 43513
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL5624
NTR-old	NTR5731
CCMO	NL55597.078.15
OMON	NL-OMON43513

Study results