Dietary restriction followed by irinotecan chemotherapy

Gepubliceerd: 04-03-2016 Laatst bijgewerkt: 15-05-2024

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

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON29351

Bron
Nationaal Trial Register

Verkorte titel
DIRINO study

Aandoening

Dietary restriction
Fasting
Metastatic colorectal carcinoma
Irinotecan

Dieetrestrictie
Vasten
Gemetastaseerd colorectaal carcinoom
Irinotecan

Ondersteuning

Primaire sponsor: Erasmus Medical Center
Overige ondersteuning: Erasmus Medical Center

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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

Onderzoeksopzet

First and second cycle of irinotecan treatment.

Onderzoeksproduct en/of interventie

Standard treatment with or without dietary restriction

Contactpersonen

Publiek

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

Wetenschappelijk

Erasmus MC Cancer Institute - Department of Internal Oncology

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‘s Gravendijkwal 230

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

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

• 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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

• 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

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	11-03-2016
Aantal proefpersonen:	18
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Toelichting
Data can be requested by emailing the investigator

Ethische beoordeling

Positief advies

Datum:	04-03-2016

Soort: Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 43513
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten