The Pharmacokinetics of an oral uracil dose in patients with colorectal carcinoma.

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Dihydropyrimidine Dehydrogenase (DPD) is the initial and rate-limiting enzyme in the metabolism of 5-fluorouracil (5-FU). Patients with a partial or complete DPD deficiency are at risk to develop severe toxicity after 5-FU administration. Uracil is...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON28016

Bron
Nationaal Trial Register

Verkorte titel
KINURA-2

Aandoening

DPD deficiency
Pharmacokinetics
colorectal
DPD deficiëntie
kinetiek
uracil
colorectaal

Ondersteuning

Primaire sponsor: Leveste Scheper ziekenhuis
Leids Universitair medische Centum
Leveste Scheper Ziekenhuis
Boermarkeweg 60

7824 AA Emmen

Postadres
Postbus 30.002
7800 RA Emmen
Overige ondersteuning: fund = initiator = sponsor

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Compare the AUC of uracil in patients with metastatic colorectal disease and patients with adjuvant treatment.

Toelichting onderzoek

Achtergrond van het onderzoek

Background of the study:

Dihydropyrimidine Dehydrogenase (DPD) is the initial and rate-limiting enzyme in the metabolism of 5-fluorouracil (5-FU).

Patients with a partial or complete DPD deficiency are at risk to develop severe toxicity after 5-FU administration. Uracil is
degraded in dihydrouracil in a similar way as 5-FU. Hypothetically, DPD deficiency may cause higher uracil levels and a reduced
turnover of uracil into dihydrouracil. An oral uracil test dose might be useful to determine the systemic DPD activity by measuring
uracil and its metabolite dihydrouracil in plasma.

Objective of the study:

To compare the pharmacokinetic profile of uracil in cancer patients and healthy volunteers.

Study design:

Case control PK study with 24 patients diagnosed with colorectal cancer.

Study population:

Cancer patients with or without metastasis, age > 18 jaar, DPD activity in PBMC ? 6 nmol/mg/hour treated with 5-FU or
capecitabine.

Intervention:

An oral dose of 500 mg/m2 is adminstered to patients. Bloodsamples are obtained just before and on several timepoints after
dosage.

Primary study parameters/outcome of the study:

AUC of uracil. The second objective of the study is to determine if there is a interpatient correlation between uracil levels
determined in blood sampled with a newly developed bloodspot method and venapunction.

Doel van het onderzoek

Dihydropyrimidine Dehydrogenase (DPD) is the initial and rate-limiting enzyme in the metabolism of 5-fluorouracil (5-FU). Patients with a partial or complete DPD deficiency are at risk to develop severe toxicity after 5-FU administration. Uracil is degraded in dihydrouracil in a similar way as 5-FU. Hypothetically, DPD deficiency may cause higher uracil levels and a reduced turnover of uracil into dihydrouracil. An oral uracil test dose might be useful to determine the systemic DPD activity by measuring uracil and its metabolite dihydrouracil in plasma.

Onderzoeksopzet

t = 0, 15, 30, 45, 60, 80, 100, 120, 150, 180 en 240 minutes after intake of uracil.

Onderzoeksproduct en/of interventie

An oral dose of 500 mg/m2 is adminstered to patients. Bloodsamples are obtained just before and on several timepoints after dosage.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age > 18 year;

2. Metastatic disease or adjuvant treatment;

3. Signed informed consent;

4. DPD activity in PBMCs ≥ 6 nmol/mg/hr;

5. Live expectation > 3 months.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. DPD activity in PBMCs < 6 nmol/mg/hr;

2. Pregnancy;

3. Breasfeeding;

4. The use of Cimetidine (regarding drug interactions with 5-fluorouracil and capecitabine);

5. Reduced renal function (creatinine clearance <50 ml/min, calculated with the Cockcroft&Gault formula).

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	05-08-2011
Aantal proefpersonen:	24
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	12-04-2012
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3243
NTR-old	NTR3395
Ander register	EudraCT : EudraCT2009-017620-11
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A