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

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON28016

Source
Nationaal Trial Register

Brief title
KINURA-2

Health condition

DPD deficiency
Pharmacokinetics
colorectal
DPD deficiëntie
kinetiek
uracil
colorectaal

Sponsors and support

Primary sponsor: Leveste Scheper ziekenhuis
Leids Universitair medische Centum
Leveste Scheper Ziekenhuis
Boermarkeweg 60
7824 AA Emmen

Postadres

Postbus 30.002
7800 RA Emmen
Source(s) of monetary or material Support: fund = initiator = sponsor

Intervention

Outcome measures

Primary outcome

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

Secondary outcome

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 mehthod and venapunction.AUC of uracil.

Study description

Background summary

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.

Study objective

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.

Study design

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

Intervention

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

Contacts

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Eligibility criteria

Inclusion criteria

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.

Exclusion criteria

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).

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-08-2011
Enrollment:	24
Type:	Anticipated

Ethics review

Positive opinion

Date:	12-04-2012
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	NL3243
NTR-old	NTR3395
Other	EudraCT : EudraCT2009-017620-11
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A