Effect of dosing time on the pharmacokinetics and pharmacodynamics of sunitinib

Gepubliceerd: 12-07-2012 Laatst bijgewerkt: 13-01-2025

Amendment (5-apr-2013): Dosing-time of sunitinib may alter the pharmacokinetics

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

Samenvatting

ID

NL-OMON20106

Bron
NTR

Aandoening

Patients with advanced clear cell renal cell carcinoma, metastatic GIST or advanced p-NET treated with sunitinib

Ondersteuning

Primaire sponsor: Erasmus Medical Center, Department of Medical Oncology
Overige ondersteuning: self financial research

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Difference in pharmacokinetics of sunitinib in morning intake compared to evening intake.

Toelichting onderzoek

Achtergrond van het onderzoek

Since metabolism of sunitinib is dependant of different cytochrome P450 enzymes, including CYP3A4, which in cell-lines and rodents show a circadian rhythm in expression, it is very likely that pharmacokinetics of sunitinib is time dependant. The activity of CYP3A4 probably drops in night time. Higher concentrations of sunitinib and its active metabolite may be reached when sunitinib is taken in the evening.
Patients participating in this cross-over study will be followed, during two courses of sunitinib. In one of both courses, they will take sunitinib at 08.00 AM, and during the other course at 18.00 PM. During both courses, they will behospiatlized during 24 hours for pharmacokinetic measurements of sunitinib.
To investigate the circadian rhythm of CYP3A4, patients will be administered a low dose of midazolam. Pharmacokinetics of midazolam and 1OH-midazolam will be measured. In addition, also the endogenous marker 4beta-hydroxycholesterol will be studied as an extra test to study CYP3A4 dynamics.
After completing these two courses, patients are free to decide at wich time they will continue sunitinib intake.

Amendment: Since metabolism of sunitinib is dependant of different cytochrome P450 enzymes, including CYP3A4, which in cell-lines and rodents show a circadian rhythm in expression, it is very likely that pharmacokinetics of sunitinib is time dependant. Exposure to sunitinib may therefore be influenced by dosing-time.

Patients participating in this cross-over study will be followed, during three courses of sunitinib. In one of three courses, they will take sunitinib at 08.00, one course at 18.00, and one course at 13.00 . During all three courses, they will behospiatlized during 24 hours for pharmacokinetic measurements of sunitinib.

To investigate the circadian rhythm of CYP3A4, patients will be administered a low dose of midazolam. Pharmacokinetics of midazolam and 1OH-midazolam will be measured. In addition, also the endogenous marker 4beta-hydroxycholesterol will be studied as an extra test to study CYP3A4 dynamics.

After completing these three courses, patients are free to decide at wich time they will continue sunitinib intake.

Doel van het onderzoek

Amendment (5-apr-2013): Dosing-time of sunitinib may alter the pharmacokinetics

Onderzoeksopzet

2 courses of sunitinib treatment.

Onderzoeksproduct en/of interventie

1. Blood withdrawal for pharmacokinetics of sunitinib and midazolam;

2. Administration of midazolam;

3. Urine sample collection.

Contactpersonen

Publiek

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age ¡Ý 18 years;

2. Histological or cytological confirmed diagnosis of advanced clear©\cell renal cell carcinoma, GIST or pancreatic neuro©\endocrine tumor, treated with sunitinib;

3. WHO performance score ¡Ü 1 at study entry;

4. Any stable dose of sunitinib at study entry, defined as no dose change within 3 weeks prior to pharmacokinetics;

5. Adequate hematological functions (ANC > 1.0 x 109/L, platelets > 100 x 109/L);

6. Adequate liver and renal function defined as bilirubin concentration ¡Ü 2 x ULN, AST and ALT ¡Ü 2.5 x ULN, serum creatinin concentration ¡Ü 2 x ULN;

7. Written informed consent;

8. For patients with reproductive potential a reliable method of contraception (excluding oral contraceptives) must be used.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Pregnant or child nursing patients;

2. Serious illness or medical unstable condition requiring treatment, symptomatic CNS metastasis or history of psychiatric disorder that would prohibit the understanding and giving of informed consent;

3. Major surgery within 2 weeks prior to start of the protocol;

4. Use of CYP3A4 inhibiting or inducing medication;

5. Patients who are unable to collect blood from;

6. Patients with known allergy to sunitinib or midazolam;

7. Patients unwilling or unable to give written informed consent.

Onderzoeksopzet

Opzet

Type: Observationeel onderzoek, zonder invasieve metingen

Onderzoeksmodel:	Parallel
Toewijzing:	Niet-gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	10-07-2012
Aantal proefpersonen:	18
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	12-07-2012
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 39190
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3378
NTR-old	NTR3526
Ander register	METC ErasmusMC : 12-138
CCMO	NL39931.078.12
OMON	NL-OMON39190

Resultaten

Samenvatting resultaten

Kloth et al. Relationship Between Sunitinib Pharmacokinetics and Administration Time: Preclinical and Clinical Evidence. Clin Pharmacokinet. 2015;54(8):851-8