The influence of probenecid on the metabolism of sorafenib

No registrations found.

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

Summary

ID

NL-OMON21261

Source
Nationaal Trial Register

Brief title
PROSORA

Health condition

Hepatocellular carcinoma
thyroid carcinoma
renal cell carcinoma
HCC, hepatocellulair carcinoom
RCC, Niercelcarcinoom
Schildkliercarcinoom

Sponsors and support

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

Intervention

Outcome measures

Primary outcome

To demonstrate bioequivalence of sorafenib with probenecid relative to sorafenib without probenecid based on the AUC in patients with unresectable hepatocellular cancer, advanced clear-cell renal cell carcinoma, locally recurrent or metastatic, progressive, differentiated thyroid carcinoma refractory to radioactive iodine treatment.

Secondary outcome

1. Other pharmacokinetic outcomes (i.e. clearance, maximum concentration (Cmax), Maximum steady-state concentration (Cmaxss), Minimal concentration (Cmin), steady-state volume of distribution (Vss) and half-life (t½)).

2. To evaluate the incidence and severity of side-effects of treatment with sorafenib in absence and presence of probenecid (in particular HFSR) .

3. To evaluate the intracellular concentration of sorafenib in skin in patients treated with sorafenib in absence and presence of probenecid.

4. To determine the influence of HFSR on quality of life

Study description

Background summary

In this study we want to determine the safety and influence on pharmacokinetics of sorafenib by probenecid. As a secondary outcome we study the influence on HFSR.

Study objective

We want to determine the influence and safety of probenecid on sorafenib pharmacokinetics. By inhibiting the OAT6 transporter there might be a faborable effect on Hand-foot syndrome

Study design

Pharmacokinetics and skin-biopsies will be taken at day 1 and day 15. Also an HFSR QoL questionnaire will be taken out at registration, day 1 and day 15.

Intervention

sorafenib alone vs sorafenib + probenecid for 14 consecutive days

Contacts

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Eligibility criteria

Inclusion criteria

1. Age ≥ 18 years

2. Histological or cytological confirmed diagnosis of mRCC, HCC or differentiated thyroid carcinoma

3. Start of sorafenib therapy, at least 7 days but nog longer than 14 days prior to start of the study NB. Patients are allowed to have had previous sorafenib therapy or have started with sorafenib.

4. WHO Performance Status ≤ 2 (appendix D)

5. Able and willing to sign the Informed Consent Form prior to screening evaluations

6. Adequate organ function as defined by:

a. Total bilirubin ≤ 1.5 x ULN (except in case of documented Gilbert’s disease)

b. ASAT ≤ 3.0 x ULN (or ≤ 5 x ULN if liver metastases are present)

c. ALAT ≤ 3.0 x ULN (or ≤ 5 x ULN if liver metastases are present)

d. Serum creatinin ≤ 1.5 x ULN

7. Adequate baseline patient characteristics (complete blood count, and serum biochemistry which involves sodium, potassium, creatinin, calculation of creatinin clearance (MDRD), amylase, lipase, calcium, phosphate, AST, ALT, gamma glutamyltranspeptidase (□-GT), lactate dehydrogenase (LDH), ALP, total bilirubin, albumin).

Exclusion criteria

1. Use of drugs which may show an increased systemic exposure when taken concomitantly with probenecid. (see appendix C)

2. Patients with known blood dyscrasias, uric acid kidney stones or until an acute gouty attack has subsided.

3. Use of (over the counter) medication or (herbal) supplements which can interact with either sorafenib or probenecid, e.g. by induction or inhibition of CYP3A4, UGT1A9 (see appendix B and C)

4. Unable or unwilling to abstain from grapefruit, grapefruit juice, herbal dietary supplements, and herbal tea during the study

5. Previous use of probenecid during the last 2 weeks prior to sorafenib treatment

6. Contraindications for use of probenecid such as acute gouty attack or porphyria.

7. Unwilling to undergo a skin biopsy

8. A BMI (body mass index) of less than 8.5 and more than 35.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-11-2017
Enrollment:	16
Type:	Actual

IPD sharing statement

Plan to share IPD: No

Ethics review

Positive opinion

Date:	22-01-2018
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	NL6783
NTR-old	NTR6967
Other	METC Erasmus MC : MEC 17-490

Study results