Population pharmacokinetics and pharmacodynamics of sorafenib in hepatocellular carcinoma patients with Child Pugh B liver cirrhosis

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1. To optimize sorafenib treatment in patients with HCC and CP-B liver cirrhosis by exploration of sorafenib exposure, its variability and predictive factors .Secondary:2. To assess the relation between sorafenib exposure and both toxicity and...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatic and hepatobiliary disorders
Study type	Interventional

Summary

ID

NL-OMON44524

Source
ToetsingOnline

Brief title
Sorafenib pharmacokinetics in Child Pugh B liver cirrhosis (SORBE)

Condition

- Hepatic and hepatobiliary disorders
- Hepatobiliary neoplasms malignant and unspecified

Synonym
hepatocellular carcinoma, liver cancer

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Bayer

Intervention

Keyword: liver cirrhosis, pharmacokinetics, sorafenib

Outcome measures

Primary outcome

1. Exposure and intra- and inter-patient variability in exposure to sorafenib

and its metabolites

2. Identification of predictive factors for sorafenib exposure, i.e. bilirubin,

CYP3A4 activity

Secondary outcome

3. Correlation between sorafenib exposure and adverse events and progression

free survival

4. Difference in exposure to 5 CYP probe drugs following administration of an

oral cocktail of these agents after 4 weeks of sorafenib treatment in

comparison with exposure to these cocktail probe drugs before initiation of

sorafenib (substudy in 15 patients)

Study description

Background summary

Sorafenib has proven efficacy in advanced hepatocellular carcinoma (HCC). Most patients with HCC have impaired liver function due to underlying liver cirrhosis. The severity of liver cirrhosis might have implications on sorafenib metabolism. To date, no data showing unequivocal activity and tolerability of sorafenib in patients with moderate cirrhosis (Child-Pugh (CP)-B) have been

published.
To specifically address this issue, this study aims to explore population pharmacokinetics of sorafenib and to explore the relationship between sorafenib exposure and its efficacy and toxicity in CP-B patients with irresectable HCC.

Study objective

1. To optimize sorafenib treatment in patients with HCC and CP-B liver cirrhosis by exploration of sorafenib exposure, its variability and predictive factors .

Secondary:
2. To assess the relation between sorafenib exposure and both toxicity and efficacy
3. To assess possible interaction between sorafenib and other CYP enzyme activity

Study design

This is a prospective, open-label, national, multicenter observational study to investigate the tolerability, pharmacokinetics and clinical activity of sorafenib and its metabolites in patients with HCC and CP-B liver cirrhosis

Intervention

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Study burden and risks

Enrolled patients will be admitted in the hospital for tree 8h visits for pharmacokinetic (PK) sampling of sorafenib and midazolam or the drug cocktail (used for CYP phenotyping). All PK blood samples will be drawn via an intravenous catheter. The total amount of blood taken will be ca 70 ml. The risks of these procedures are low.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

advanced hepatocelllar carcinoma (HCC) - BCLC stage C
Child Pugh(CP)-B liver cirrhosis (CP-B score 7 or 8)

Exclusion criteria

Child Pugh-B9 liver cirrhosis
Child Pugh-C liver cirrhosis
Concurrent antitumoral treatment for HCC or other malignancies

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-07-2014
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO Date:	15-05-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-11-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-08-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
CCMO	NL48419.018.14