Phase I dose escalation study with sorafenib in combination with sirolimus in patients with solid tumor.

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Primary:To identify the recommended dose of sorafenib and of sirolimus for combination therapy in subsequent phase II trials Secondary:1. to determine the safety profile of the combination therapy of sorafenib with sirolimus.2. to determine, if...

Ethical review	Approved WMO
Status	Pending
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON30326

Source
ToetsingOnline

Brief title
Phase I study with sorafenib and sirolimus

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
malignant solid tumors

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Bayer,dit is een investigator initiated studie

waarvoor een "grant" door de industrie is gegeven

Intervention

Keyword: phase I, sirolimus, solid tumors, sorafenib

Outcome measures

Primary outcome

Critria for evaluation

Safety profile

The primary end point is to identify the recommended doses for the combination

of sorafenib and sirolimus for subsequent phase II studies.

Evaluation of DLT*s will be done. Adverse events will be scored using CTC AE v3.

Efficacy

There will be a descriptive analysis of proportion of patients with response or

stable disease.

Secondary outcome

not applicable

Study description

Background summary

Sirolimus, a raf kinase inhibitor, is a recently registered anti cancer drug for renal cell cancer. Sorafenib is a mTOR inhibitor. mTOR inhibitors can induce an anti-tumor effect. The sirolimus - sorafenib combination therapy will be studied in the present trial in patients with advanced refractory solid tumours for whom no standard therapy exists. It is hypothesized that the combination of sorafenib with sirolimus, two targeted drugs, could work synergistic in inhibiting tumor growth. The reason for choosing sirolimus and not temsirolimus (CCI-779), another mTOR inhibitor, is that both sorafenib and sirolimus are tablets for oral use. Temsirolimus can be administered parenterally only.

Because sorafenib and sirolimus are both metabolized via CYP3A4 the pharmacokinetics can be influenced by each other. Thus, a close monitoring of safety and toxicity as well as exact monitoring of pharmacokinetics of sirolimus and sorafenib will be performed.

Study objective

Primary:
To identify the recommended dose of sorafenib and of sirolimus for combination therapy in subsequent phase II trials
Secondary:
1. to determine the safety profile of the combination therapy of sorafenib with sirolimus.
2. to determine, if possible, the Maximum Tolerated Dose (MTD) of sorafenib and sirolimus in combination therapy
3. to analyze pharmacokinetic PK profiles (AUC, Cmax) during combination therapy for sorafenib and sirolimus
4. to evaluate efficacy of the combination descriptively (response rate and rate of stable diseases)

Study design

Mono-centre, open-label, uncontrolled, dose-escalating phase I design
The design includes up to 3 treatment cohorts with 6 patients each.

Intervention

Combination of sorafenib with sirolimus (dose escalating study)

Study burden and risks

This is a phase I study. Sorafenib is registered for the use in renal cell cancer. Sirolimus is registered for another indication than cancer. The dosages needed to have clinical effect are well known. In the first cohort of patients we treat at a lower dosage than the normal dosages used for both sorafenib and sirolimus. Thus the risk for serious adverse events is limited.
The response rate in phase I studies is 10% in general.

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

1. Patients with histological or cytological confirmed advanced solid tumor, which is refractory to standard therapies or for which no standard therapy exists and for which there is a rationale for the therapeutic use of a combination of sorafenib and sirolimus (especially metastic RCC, malignant melanoma, HCC, NSCLC, pancreatic cancer, hormone refractory prostate cancer).
2. Men or women of at least 18 years
3. Patients who have an ECOG status of 0 or 1
4. Patients who have a life expectancy of at least 12 weeks
5. Adequate bone marrow, liver and renal function

Exclusion criteria

1. History of serious cardiac disease
2. Active clinically serious bacterial, viral or fungal infections (> grade 2).
3. Known history of human immunodeficiency virus (HIV) infection or chronic hepatitis B or C.
4. Clinically symptomatic brain or meningeal metastasis.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2007
Enrollment:	18
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Nexavar
Generic name:	Sorafenib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Rapamune
Generic name:	Sirolimus
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	04-01-2007
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-09-2007
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-03-2008
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-09-2008
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EudraCT	EUCTR2006-006454-10-NL
CCMO	NL15796.091.06