Hepatocellular carcinoma: vascular abnormalities prior to, during and following systemic anti-cancer treatment

Published: 07-01-2009
Last updated: 06-05-2024

To determine the efficacy of the combination of everolimus and capecitabine in a group of patients with metastatic or locally advanced HCC with Child-Pugh class B liver cirrhosis. In addition, to investigate biomarkers of HCC before and during the...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON32482

Source
ToetsingOnline

Brief title
geen

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
liver cancer

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: capecitabine, everolimus, hepatocellular carcinoma, systemic anti-cancer treatment

Outcome measures

Primary outcome

1. Progression-free survival (PFS) at 6 months measured by CT-scan at 3-months

intervals

2. Assessment of circulating levels of microparticles derived from vascular

and/or tumour cells, and plasma microparticles-tissue factor activity

3. Circulating levels of biomarkers of the vasculature including endothelium

activation marker such as VCAM, L-CAM, and P-selectin

4. Investigation whether 2 and 3 are predictive factors for PFS and overall

survival

Secondary outcome

1. Objective complete and partial response rate (RECIST criteria)

2. Overall survival

3. One year survival rate

4. Safety

5. Alterations in cellular source of circulating MP during treatment as

compared to pretreatment MP phenotype.

6. Assessment of development of venous thromboembolic events

Study description

Background summary

Despite many drugs tested in patients with advanced hepatocellular carcinoma (HCC), progress has been limited and all patients for whom no surgical and/or transplantation options exist will succumb of the disease. Capecitabine as one of the few chemotherapeutic agents has demonstrated limited activity and efficacy in patients with metastatic HCC. Sorafenib is recently registered as the first and until now the only effective systemic therapy for patients with HCC with Child-Pugh class A liver cirrhosis. However, currently there is no effective systemic therapy available for patients with Child-Pugh class B of C liver cirrosis. Therefore, exploration of novel strategies is necessary. One of these possibilities is the use of mTOR inhibitors either alone or in combination with cytostatic drugs, as the AKT-mTOR pathway has recently been shown to be deregulated in most cases of HCC. Everolimus is a compound with mTOR inhibitory activity that has been widely used in liver, heart, and renal transplantation setting, and which now -as other mTOR inhibitors- attracts wide attention for use in patients with metastatic malignancies. The i.v. compound Temsirolimus, and one oral analogue everolimus (RAD001) have already demonstrated marked activity in for instance renal cell carcinoma.

We propose a everolimus and capecitabine combination regimen in which the dose of capecitabine will be much lower than what has been used in the treatment of colorectal cancer, in order to allow dosing with expected mild to only moderate side effects. In addition, the combination of two oral compounds is attractive in terms of quality of life benefits, fewer hours spend traveling to clinics and waiting, and no administration visits compared to i.v. chemotherapy.

Study objective

To determine the efficacy of the combination of everolimus and capecitabine in a group of patients with metastatic or locally advanced HCC with Child-Pugh class B liver cirrhosis. In addition, to investigate biomarkers of HCC before and during the systemic treatment.

Study design

Open label, non-placebo-controlled, non-randomized study in Advanced HCC patients.

Intervention

Everolimus will be administrated daily at an oral dose of 6 mg and the dose of capecitabine will be 500 mg/m2 twice daily for 2 weeks, with one week of rest period. The treatment will be continued until disease progression, unacceptable toxicity or any other reason why continuation of the treatment is no longer in the patient*s best interest.

Study burden and risks

not applicable

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 hepatocellular carcinoom.
Child-Pugh class B liver cirrhosis.

Exclusion criteria

Major cardiac disease, HIV infection, serious active infectie

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-07-2009
Enrollment:	28
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Certican
Generic name:	everolimus
Registration:	Yes - NL outside intended use

Product type:	Medicine
Brand name:	Xeloda
Generic name:	capecitabine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	07-01-2009
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	09-01-2009
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2008-003972-23-NL

Register	ID
CCMO	NL24012.058.08