A multicenter, open label, phase I / II study to evaluate safety, pharmacokinetics and efficacy of BIBF 1120 in comparison with oral sorafenib for advanced hepatocellular carcinoma patients.

Published: 17-01-2012
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To evaluate the efficacy and safety of BIBF 1120 in HCC patients without prior systemic treatment as compared to Sorafenib.

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

Summary

ID

NL-OMON39531

Source
ToetsingOnline

Brief title
BIBF 1120 in HCC

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
hepatocellular carcinoma, liver cancer

Research involving
Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Boehringer Ingelheim bv

Intervention

Keyword: BIBF 1120, hepatocellular carcinoma, Sorafenib

Outcome measures

Primary outcome

Primary endpoint is time to progression.

Secondary outcome

Secundary endpoins are:

-safety of BIBF 1120

-Dose Limiting Toxicities

-Pharmacokinetics

-objective RECIST 1.0 tumor response

-Overall survival

Study description

Background summary

Hepatocellular carcinoma (HCC) is the fifth most common and fourth most lethal tumour in the world. Risc factors are hepatitis B and C virus infection, alcohol abuse and possible life style associated steatofibrosis (fatty liver). HCC is a hypervasculare tumour in which various angiogenesis growth factors are over represented. This is the basis for a treatment of HCC with angiogenesis inhibitors, such as sorafenib and BIBF 1120. In 2007 Sorafenib was registered for the use as first line treatment in advanced HCC with a median overall survival of 3 months. BIBF 1120 is a more potent inhibitor of angiogenesis than sorafenib. Also BIBF 1120 possibly has e less, or at least other toxicity thn sorafenib.

Study objective

To evaluate the efficacy and safety of BIBF 1120 in HCC patients without prior systemic treatment as compared to Sorafenib.

Study design

This study consists of two parts of which only the hase II part will take place in the Netherlands.
The Phase II part is an open label, randomised study in which the treatment with sorafenib is compared to BIBF 1120 in a parallel group design.

The patients come for a first screen visit to the physician. In case they qualify according to the study criteria for participation treatment will be started as of visit 2. Patients will then regularly (every 1st and 15th day of each treatment cycle) be checked. Details are in the flowchart in the protocol. Tumour response is regularly evaluated according to RECIST 1.0 criteria.

Patients will stop study medication at the time of disease progression or toxicity.

Intervention

Patents are treated with Sorafenib or BIBF1120.

Study burden and risks

The standard treatment for these patients is currently treatment with Sorafenib. Sorafenib has an effect in the treatment of HCC. This effect was however temporary. Momentarily there is no other systemic treament option available for patients with advanced HCC. Possibly BIBF1120 has a more potent effect due to the specific angiogenesis inhibition. Clinical benefit of the treatment is followed closely by the making of scans.

Patients without clinical benefit, with a progression of the tumour, will be stopped treatment of BIBF1120. These patients can then still be treated with Sorafenib. Treatment with BIBF1120 might be a benefit for these patients as an additional therapy.

Adverse events of BIBF1120 are primarily gastro-intestinal: nausea, vomiting, diarrhoea and abdominal pain. Also a reversible increase of liver enzymes appears and fatigue, asthenia and anorexia.

Side effects can be reduced by a dose reduction of BIBF1120 or a symptomatic treatment. Laboratory values are regularly checked.

Taken together, patients with advanced HCC may benefit from tumour shrinkage or stabilization and alleviation of disease-related symptoms.

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. HCC, either histologically/cytologically confirmed diagnosis or clinically diagnosis by ;AASLD criteria, which is not amenable to local therapy (RFA, PEI, RT, TACE);2. Age 18 years or older;3. ECOG performance score of 2 or less;4. Child-Pugh score A (score 5-6);5. At least one measurable lesion according to RECIST 1.0 (this criterion is limited to phase II only);6. In case a measurable lesion was previously treated by loco-regional therapy (RFA, PEI, TACE or RT), this lesion must be documented as progression according to RECIST 1.0 by CT or MRI (this criterion is limited to phase II only).;7. Time interval from last local therapy more than 4 weeks prior to start of study;treatment;8. Written informed consent consistent with ICH-GCP

and local legislation

Exclusion criteria

1. Prior systemic therapy for metastatic/unresectable HCC (for phase II) ;2. More then one line of prior systemic therapy for metastatic/unresectable HCC (for ;phase I);3. Fibrolamellar HCC;4. Uncontrolled or refractory ascites by adequate medical therapy;5. Bilirubin greater than 1.5 times ULN;6. AST or ALT greater than 2 times ULN;7. Hepatic encephalopathy more than grade 1 according to Child-Pugh criteria;8. Prothrombin time international normalized ratio greater than 2.3, or prothrombin ;time more than 6 seconds prolonged than control;9. Absolute neutrophil count less than 1000/µL;10. Platelet count less than 60000/µL;11. Hemoglobin less than 9 g/dL;12. Serum creatinine greater than 1.5 times ULN;13. Proteinuria of CTCAE grade 2 or greater;14. Variceal bleeding within 6 months prior to start of study treatment;15. History of major thrombotic (except portal vein thrombosis) or clinically relevant ;major bleeding event in the past 6 months;16. Known inherited predisposition to bleeding or thrombosis ;17. Significant cardiovascular diseases (i.e. hypertension not controlled by medical ;therapy (blood pressure > 150/90 mmHg), unstable angina, history of myocardial ;infarction within the past 6 months, congestive heart failure > NYHA II, serious ;cardiac arrhythmia, pericardial effusion);18. Therapeutic anticoagulation (except low dose heparin and/or heparin flush as ;needed for maintenance of an indwelling intravenous device) or antiplatelet ;therapy (except for chronic low-dose therapy with acetylsalicylic acid <= 325mg ;per day);19. Last administration of systemic treatment for HCC within 4 weeks prior to start ;of study treatment or no recovery from any treatment related toxicity;20. Major surgery within 4 weeks prior to start of study treatment;21. Treatment with other investigational drugs concomitantly with this trial (except ;for present trial drug);22. Serious illness or concomitant non-oncological disease such as neurologic, ;psychiatric, infectious disease or active ulcers (gastro-intestinal tract, skin) or ;laboratory abnormality that may increase the risk associated with study ;participation or study drug administration and in the judgment of the ;investigator would make the patient inappropriate for entry into the study;23. Patients who are sexually active and unwilling to use a medically acceptable ;method of contraception (e.g. such as implants, injectables, combined oral ;contraceptives, some intrauterine devices or vasectomized partner for ;participating females, condomes for participating males) during the trial and for ;at least twelve months after end of active therapy;24. Current alcohol abuse or drug abuse that would limit patient ability to comply ;with protocol;25. Symptomatic CNS metastasis;26. Life expectancy less than 12 weeks;27. Patient unable to take oral medication;28. Gastrointestinal disorders or abnormalities that would interfere with absorption ;of the study drug;29. Pregnancy or breast feeding;30. Patient unable to comply with the protocol;31. Other malignancy within the past three years other than basal cell skin cancer, ;or carcinoma in situ of the cervix;32. Hypersensitivity to active substance or to any of the excipients of both BIBF ;1120 or sorafenib

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-09-2012
Enrollment:	1
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nintedanib
Generic name:	nvt
Product type:	Medicine
Brand name:	Sorafenib
Generic name:	Nexavar
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	17-01-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-06-2012
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-07-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-08-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	20-08-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	20-09-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	25-10-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	26-10-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	18-12-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	11-02-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-05-2014
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	10-06-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-09-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	19-09-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-04-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-04-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2009-011925-14-NL
CCMO	NL38928.041.12