A phase II study of cediranib as palliative treatment in patients with symptomatic malignant ascites or pleural effusion

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Primary objective:To assess the puncture free survival after start of treatment with cediranib (time to first need for paracentesis or thoracentesis or time to death, which event occurred first)Secondary objectives:-To assess the palliative effects...

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

Summary

ID

NL-OMON35120

Source
ToetsingOnline

Brief title
cediranib as palliative treatment of malignant ascites or pleural effusion

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
excess fluid in the pleural cavity, peritoneal cavity fluid

Research involving
Human

Sponsors and support

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

Intervention

Keyword: cediranib, malignant ascites, malignant pleural effusion

Outcome measures

Primary outcome

If the puncture free survival after start of treatment with cediranib (time to first need for paracentesis or thoracentesis or time to death, which event occurred first) is more than 44 days the treatment of ascites and/or pleural effusion with cediranib is effective.

Secondary outcome

n.a.

Study description

Background summary

Malignant ascites is a difficult clinical problem. Increasing intra-abdominal pressure resulting from fluid accumulation may cause anorexia, sleep disturbance, pain, dyspnoea, abdominal distension, fatigue, nausea vomiting and reduced mobility. The main complaints of pleural effusion are dyspnoea and cough. Paracentesis and thoracentesis provide relief for a very limited period. Studies have shown high concentrations of VEGF in malignant ascites and pleural effusion. Beneficial effects of treatment with an intravenous or intraperitoneal antibody against VEGF on malignant ascites have been reported. In the recent past we have treated two patients with symptomatic malignant ascites (colorectal cancer and ovarian cancer, respectively) in a phase I study with cediranib. Shortly after start of cediranib, within a couple of days, the ascites disappeared. However, after stopping cediranib for progressive disease on other sites the ascites reappeared within days. Therefore, one of those patients was treated with cediranib as palliative treatment until two days before his death, which was beneficial for this patient.
In this phase II study we would like to investigate the effects of treatment with cediranib as palliative treatment on malignant ascites or pleural effusion.

Study objective

Primary objective:
To assess the puncture free survival after start of treatment with cediranib (time to first need for paracentesis or thoracentesis or time to death, which event occurred first)

Secondary objectives:
-To assess the palliative effects of cediranib on ascites and ascites related symptoms or to assess the palliative effects of cediranib on pleural effusion and pleural effusion related symptoms
-The effect of treating ascites and/or pleural effusion with cediranib on the quality of life
-Toxicity profile of cediranib (acute and late adverse events) in this group of patients
-Tumour response
-Overall survival

Study design

This will be an open label, randomized phase II single centre study. Sixteen patients with ascites and 16 patients with pleural effusion will be randomized between immediate start with cediranib or best supportive care and start with cediranib after 4 weeks. Cross-over from the control group to the cediranib arm is permitted when paracentesis or thoracentesis is necessary before start of Cediranib on day 29.

Intervention

The start dosage of cediranib will be 30 mg oid. The dose will be titrated to have the most beneficial effect on the ascites or pleural effusion and the fewest adverse events. Special in this study is the possibility to decrease (to minimal 15 mg oid) or increase the dose (to a maximum of 30 mg oid) during the study to get an individualised optimal palliative treatment with cediranib. The patient will continue cediranib as long as a clinical benefit is experienced.
Half of the patients start with cediranib 30 mg once a day and best supportive care, the other half will have the first 28 days of the study just best supportive care and will start after 28 days with cediranib 30 mg once a day

Study burden and risks

For the exact burden of the study see the table in the protocol on page 18 and 19.

In former studies, doses of 30 mg cediranib were well tolerated in patients with advanced cancer.

We think that cediranib can be an effective drug in the palliative treatment of

malignant ascites or pleural effusion and that it can improve the quality of life of this group of patients. We specifically chose in this study for a lower dose cediranib than used in former studies because we expect that cediranib is also effective in a lower dose and that with the lower dose the side effects will restricted.

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

-symptomatic malignant ascites and/or pleural effusion (from a histological proven solid malignancy which is refractory to standard anti-tumour therapy of for which no standard therapy exists)
-Karnofsky score >= 50 if the low performance score is due to ascites and/or pleural effusion, otherwise >= 60;-written informed consent

Exclusion criteria

Contraindications for treatment with cediranib:
-The presence of a pleural or peritoneal tap
-Untreated unstable brain or meningeal metastases.
-Previous treatment with chemotherapeutic agents or tyrosine kinase inhibitors (TKIs) within 14 days prior to the first dose of cediranib, with cetuximab within 30 days prior to the first dose of cediranib, or with bevacizumab within 60 days prior to the first dose of cediranib
-Inadequate bone marrow reserve as demonstrated by an absolute neutrophil count <=1.5 x 109/L or platelet count <=100 x 109/L
-Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >= 2,5 x ULN
-Serum creatinine > 1.5 x ULRR or a creatinine clearance of <= 50mL/min calculated by Cockcroft-Gault
-Greater than +1 proteinuria on two consecutive dipsticks taken no less than 1 week apart unless urinary protein < 1.5g in a 24 hr period
-Prothrombin time (PT) and activated partial thromboplastin time (APTT) > 2 x ULN History of significant gastrointestinal impairment, as judged by the Investigator, that
would significantly affect the absorption of cediranib, including the ability to swallow the tablet whole. Patients with an ileostoma.
- Patients with a history of poorly controlled hypertension with resting blood pressure >150/100 in the presence or absence of a stable regimen of anti-hypertensive therapy. Patients who are currently receiving maximal doses of calcium channel blockers or more than 1 antihypertensive for the treatment of hypertension are also ineligible.
-Any evidence of severe or uncontrolled diseases e.g., unstable or uncompensated respiratory, cardiac, hepatic or renal disease.
-Unresolved toxicity > CTC grade 1 from previous anti-cancer therapy (including radiotherapy) except alopecia (if applicable) or polyneuropathy.
-Mean QTc with Bazetts correction >470msec in screening ECG or history of familial long QT syndrome
-Significant haemorrhage (>30mL bleeding/episode in previous 3 months) or haemoptysis (>5mL fresh blood in previous 4 weeks)
-Recent (<14 days) major surgery prior to entry into the study, or a surgical incision that is not fully healed
-Pregnant or breast-feeding women or women of childbearing potential with a positive pregnancy test prior to receiving study medication
-Known risk of the patient transmitting HIV, hepatitis B or C via infected blood
-Treatment with an investigational (non-registered) drug within 30 days prior to the first dose of cediranib
-Other concomitant anti-cancer therapy (including LHRH agonists) except steroids
-Concomitant use of any medication that may significantly affect hepatic cytochrome P450 drug metabolising activity by way of enzyme induction (e.g., phenytoin) or inhibition (e.g., ketoconazole, ritonavir, erythromycin) within 2 weeks if the first dose of cediranib and throughout the study period
-Patients being treated with anticoagulants (with the exception of low molecular weight heparin).
-Patients previously treated with antracyclines (total of > 550 mg/m2 doxorubicine) and an

ejection fraction on the MUGA scan below 40%

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-04-2010
Enrollment:	32
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	cediranib
Generic name:	recentin

Ethics review

Approved WMO Date:	03-02-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-03-2010

Application type:	First submission
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	EUCTR2010-018275-20-NL
CCMO	NL31254.091.10