Pharmacokinetics of bevacizumab in patients with malignant ascites

Published: 17-12-2008
Last updated: 07-05-2024

To study pharmacokinetics of intravenously and intraperitoneally administered bevacizumab in patients with malignant ascites for whom there is no systemic anti-tumour treatment available.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metastases
Study type	Interventional

Summary

ID

NL-OMON32123

Source
ToetsingOnline

Brief title
Pharmacokinetics of bevacizumab in patients with malignant ascites

Condition

- Metastases

Synonym
ascites

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: KWF,Roche

Intervention

Keyword: ascites, bevacizumab, pharmacokinetics

Outcome measures

Primary outcome

The pharmacokinetic of intravenously and intraperitoneally administered

111In-bevacizumab will be assesed in serum and ascites.

Secondary outcome

-VEGF levels in ascites and serum will be assesed.

-The efficacy of bevacizumab in malignant ascites will be assesed.

Study description

Background summary

Malignant ascites is an accumulation of fluid intra-abdominal as a result of peritonitis carcinomatosa. Patients usually complain about an extending belly, pain, decreased appetite and dyspnoea. If treatment with anti-tumor therapy is not an option, paracentesis leads to a decrease in symptoms. However, if no anti-tumor treatment is provided, fluid re-accumulation will occur. As a result, paracentesis should be performed regularly to improve the quality of life. However, paracentesis is an invasive, painful procedure, which can become technically difficult the more paracentesis have been performed.
There are several factors involved in the development and growth of tumors. Angiogenesis, the forming of new blood vessels is one of these factors. New vasculature allows tumor cells to execute their critical growth by supplying the tumor with nutrients and oxygen, disposal of metabolic waste products and provides route for metastatic spreading 1, 2. An important factor involved in angiogenesis is VEGF-A. VEGF-A is released by tumor cells and induces tumor neovascularization. Over-expression of VEGF-A occurs in many human tumor types. The local VEGF-A production leads to paracrine effects in the tumor, resulting in angiogenesis and growth exploration. In malignant ascites high levels of VEGF-A are found. Chemical molecules which can block the tyrosine kinase function of VEGF-receptors and antibodies binding to the ligand and the receptor have been developed. Bevacizumab is one of these antibodies, which has shown to be acitve in colon, breast and lungcancer.
In case reports, bevacizumab was active in the treatment of malignant ascites.

Bevacizumab was given intravenously in those patients. Whether local (intraperitoneal) administered bevacizumab is as effective remains to be investigated.

Study objective

To study pharmacokinetics of intravenously and intraperitoneally administered bevacizumab in patients with malignant ascites for whom there is no systemic anti-tumour treatment available.

Study design

This is an observational study, which studies the pharmacokinetics of intravenously or intraperitoneally administered bevacizumab in patients with malignant ascites.
Patients with malignant ascites, who do not receive systemic anti-tumour treatment, will be treated with bevacizumab therapy. The distribution kinetics of 111In-bevacizumab will be assessed. This distribution of 111In-bevacizumab can be used as a surrogate marker for the total bevacizumab distribution. The patients will receive one injection of 111In-bevacizumab in combination with a therapeutic dose of bevacizumab. Serum and ascitic fluid samples will be collected at T=30 minutes, T=60 minutes, T=3 hours, T= 6 hours, T=24 hours, T=48 hours, T=96 hours, T=120/144 hours and T=168 hours to assess pharmacokinetics. The toxicity of intraperitoneally and intravenously administered bevacizumab will be evaluated by measuring clinical and hematological parameters.

Intervention

5 patients will be given bevacizumab (therapeutic dose in combination with radioactive tracer dose) intravenously and 5 patients will be given bevacizumab intraperitoneally.

Study burden and risks

Bevacizumab will be administered in a therapeutic dose (7,5 mg/kg).
Side-effects of bevacizumab are leukopenia, diarrhea, hypertension, thrombotic events, deep thromboplebitis, pulmonary embolus, bleeding, proteinuria and gastro-intestinal bleeding. These events are for the most part mild to moderate in severity and clinically manageable (hypertension, proteinuria, minor bleeding) or occur uncommonly (wound healing complications, GI perforations and arterial thrombosis). Whether or not a tracer dose of 111In-bevacizumab can induce any adverse effect is unknown, but it is very unlikely and not expected. Although no toxicity is expected from the tracer-dose, side-effects of the therapeutic dose bevacizumab can be expected. These will be scored according to the Common Toxicity Criteria version 3.0.

Administration of the tracer dose 111In-bevacizumab entails radiation for the participating patients. It has been calculated that a dose of 10 MBq will lead to a radiation load of 1,8 mSv. For comparison purposes, a CT-abdomen will lead to a radiation dose of 10-15 mSv. The poor prognosis of this patient group (5 year survival < 1%) and the potential new information given by this study makes this radiation load acceptable.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
9713 GZ Groningen
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
9713 GZ Groningen
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Malignant ascites
2. At least 18 years of age
3. WHO performance status 0-2
4. Adequate haematological, hepatic, and renal function

5. Signed written informed consent
6. Able to comply with the protocol

Exclusion criteria

1. Patients receiving chemotherapy
2. Radiotherapy within 14 days before the start of the study of the involved area
3. Major surgery within 28 days before the initiation of the study
4. Clinically significant cardiovascular disease
5. Pregnant or lactating women. Documentation of a negative pregnancy test must be available for pre-menopausal women with intact reproductive organs and for women less than two years after menopause
6. CNS metastases (CT-scan not mandatory)
7. Treatment with any investigational drug within 30 days before the start of the study
8. Prior allergic reaction to immunoglobulins or immunoglobulin allergy

Study design

Design

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):	03-06-2009
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	bevacizumab
Generic name:	avastin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO	
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2008-001415-37-NL
CCMO	NL22423.042.08