Bevacizumab in combination with metronomic dose temozolomide in patients with relapsed high grade gliomas

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Primary Objective is to study the anti-tumor activity of the combination bevacizumab and metronomic dose temozolomide in patients with recurrent high grade gliomas. Secondary Objective is to investigate the effects of dexamethasone and bevacizumab...

Ethical review	Approved WMO
Status	Pending
Health condition type	Nervous system neoplasms malignant and unspecified NEC
Study type	Interventional

Summary

ID

NL-OMON30453

Source
ToetsingOnline

Brief title
AVATAR: Avastin and Temodal attacking relapsed glioma

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
brain tumor, Recurrent high grade glial tumors

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: bevacizumab, glioma, PFS6, temozolomide

Outcome measures

Primary outcome

The effects of the combination of Bevacizumab (10mg/kg every 3 weeks, iv) with daily Temozolomide (50 mg/m2, orally) will be compared with historical data of a matched patient group. The MRI effects of (co-) administration of dexamethasone (daily 3 dd 4 mg, orally) will be examined during the first 20 days of the experiment.

Main study parameters/endpoints: The progression free survival at 6 months (PFS6) is the main study parameter. This is about 9% in this patient group under the old treatment regimen. We expect a PFS6 of about 30% with the combination of bevacizumab and temozolomide. Therapy regimen will continue after 6 months.

Secondary outcome

- Safety

- Overall survival

- Response rate

- Changes in tumor blood flow and vascular permeability (Ktrans and rCBV values) during the first 20 days of treatment with bevacizumab in comparison with dexamethasone and the combination bevacizumab + dexamethasone.

- Levels of Circulating Endothelial Cells (CECs), Circulating Progenitor Cells (CPCs), Vascular endothelial growth factor (VEGF), Placental growth factor

(PlGF) and clotting factors in peripheral blood will be determined at different

time points

Study description

Background summary

There is no standard treatment for recurrent glioma, a disease with 14% surviving patients after 12 months. The change of chemotherapeutic temozolomide schedule from conventional to metronomic treatment may overcome temozolomide resistance in patients with recurrent glioma without any major toxicity. Administration of angiogenesis inhibitor bevacizumab leads to normalization of glioma tumor blood vessels, during a period of at least 28 days. During this normalization window, administration of a combination therapy is thought to be most effective. Therefore we combine bevacizumab with metronomic dose temozolomide treatment. Changes of intra tumoral blood flow and permeability due to bevacizumab administration are well visualized on MRI. During the first 20 days of the trial these changes will be compared to the effects of dexamethasone (co-) administration on MR Imaging.

Study objective

Primary Objective is to study the anti-tumor activity of the combination bevacizumab and metronomic dose temozolomide in patients with recurrent high grade gliomas. Secondary Objective is to investigate the effects of dexamethasone and bevacizumab combined with temozolomide on MRI blood flow and permeability of tumor vasculature in patients with recurrent high grade gliomas, during the first 20 days of the study.

Study design

The study will employ a prospective observational single centre study with multiple time measures in 30 patients with recurrent high grade glioma.

Intervention

Not applicable.

Study burden and risks

Burden and risks associated with participation are medium. Five extra visits are necessary for MRI scanning with contrast administration, combined with

blood sample collection. Every 3 weeks bevacizumab is administered by intravenous infusion. Daily temozolomide is taken orally. Side effects are monitored during the regularly scheduled outpatient clinic visits.

Contacts

Public
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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 present with histologically confirmed diagnosis of intracranial recurrent high grade glial tumor (WHO grade IV, including gliosarcomas).
2. Patients must have evidence of tumor progression following radiation and chemotherapy as measured by MRI (MRI-0 at presentation).
3. Patients may have received up to two prior chemotherapy regimens (with concurrent radiotherapy).
4. Patients may have undergone prior surgical resection and will be eligible if recovered from

the effects of surgery.
5. Patients must have adequate organ function.
6. Patients must have a Karnofsky Performance Score > 70%.
7. Patients must be > 18 years of age, with a life expectancy of greater than 8 weeks.
8. Signed informed consent from the patient or legal representative is required.

Exclusion criteria

9. Patients with inability to comply with protocol or study procedures (for example, an inability to swallow tablets).
10. Patients who have received treatment within the last 30 days with a drug that has not received regulatory approval for any indication at the time of study entry.
11. Patients receiving EIAEDs (Enzyme-inducing antiepileptic drugs). Patients must discontinue EIAEDs > 14 days prior to study enrollment.
12. Patients receiving any other anticancer therapy, any anticoagulant therapy.
13. Patients with serious concomitant systemic disorders that, in opinion of the investigator, would compromise the safety of the patient and his/her ability to complete the study.
14. Patients with prior thrombo-embolic events.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	13-02-2007
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Avastin
Generic name:	Bevacizumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Oradexon
Generic name:	Dexamethasone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Temodal
Generic name:	Temozolomide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	19-06-2007
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	EUCTR2007-000488-38-NL
CCMO	NL15598.018.07