Avastin and Temozolomide attacking Relapsed Glioma

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26843

Source
Nationaal Trial Register

Brief title
AVATAR

Health condition

glioma
bevacizumab
temozolomide
PFS6

Sponsors and support

Primary sponsor: Prof.dr. D.J. Richel
Source(s) of monetary or material Support: fund = initiator = sponsor

Intervention

Outcome measures

Primary outcome

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

1. Safety

2. Overall survival

3. Response rate

4. 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.

5. Levels of Circulating Endothelial Cells (CECs),

6. Circulating Progenitor Cells (CPCs),

7. Vascular endothelial growth factor (VEGF)

8. Placental growth factor (PlGF) 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

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. The PFS6 (progression free survival at 6 months) 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.

Intervention

The effects of the combination of Bevacizumab (10mg 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.

Contacts

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Eligibility criteria

Inclusion criteria

1. Patients present with histologically confirmed diagnosis of intracranial recurrent high grade glial tumor (WHO grade IV). Patients may be entered based on local pathology from the

original tumor specimen.

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, including the following:

a. Adequate bone marrow reserve:

Absolute neutrophil count (ANC) > 1.5 x
109/L, platelet count > 100 x 109/L, and hemoglobin > g/dL (6.21 mmol/L).

b. Hepatic: total bilirubin < 2 times the upper limit of normal (ULN); alkaline phosphatase (ALP), aspartate transaminase (AST), and alanine transaminase (ALT) < 3 x ULN.

c. Renal: Serum creatinine < 1.5 ULN.

These tests must be performed < 5 days prior to enrollment. Eligibility for hemoglobin count may be reached by transfusion.

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. Patient compliance and geographic proximity that allow for adequate follow up is required.

9. Male and female patients with reproductive potential must use an approved contraceptive method, if appropriate (for example, intrauterine device [IUD], birth control pills, or barrier device) during and for 3 months after discontinuation of study treatment. Women with childbearing potential must have a negative serum pregnancy test < 3 days prior to study enrollment.

10. Signed informed consent from the patient or legal representative is required.

Exclusion criteria

1. Patients with inability to comply with protocol or study procedures (for example, an inability to swallow tablets).

2. 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.

3. Patients receiving EIAEDs (Enzyme-inducing antiepileptic drugs). Patients must discontinue EIAEDs > 14 days prior to study enrollment. The investigator may prescribe non-EIAEDs.

4. Patients receiving any other anticancer therapy, any anticoagulant therapy.

5. Patients with serious concomitant systemic disorders (for example, active infection or abnormal Electrocardiogram indicative of cardiac disease) that, in opinion of the investigator, would compromise the safety of the patient and his/her ability to complete the study.

6. Patients with prior thrombo-embolic events.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-02-2007
Enrollment:	30
Type:	Actual

Ethics review

Positive opinion

Date:	29-05-2007
Application type:	First submission

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
NTR-new	NL959
NTR-old	NTR985
Other	: 15598
ISRCTN	ISRCTN23008679

Study results

Summary results
N/A