

# AVAstin and Temozolomide Attacking Relapsed glioma

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<b>Registration date</b> 16/07/2007	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 10/06/2021	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**  
15598

# Study information

## Scientific Title

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

## Acronym

AVATAR

## Study objectives

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 normalisation of glioma tumour blood vessels, during a period of at least 28 days. During this normalisation 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 six months.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Local medical ethics committee (Medisch Ethische Commissie Academisch Medisch Centrum Amsterdam) gave approval on the 28th March 2007 (ref: MEC 07/052 # 07.17.0453).

## Study design

Non-randomised, controlled, parallel group trial

## Primary study design

Interventional

## Secondary study design

Non randomised controlled trial

## Study setting(s)

Not specified

## Study type(s)

Not Specified

## Participant information sheet

## Health condition(s) or problem(s) studied

Relapsed glioma

## Interventions

The effects of the combination of Bevacizumab (10 mg every three weeks, intravenously [iv]) with daily Temozolomide (50 mg/m<sup>2</sup>, 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.

## **Intervention Type**

Drug

## **Phase**

Not Specified

## **Drug/device/biological/vaccine name(s)**

Bevacizumab, temozolomide

## **Primary outcome measure**

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 six months.

## **Secondary outcome measures**

1. Safety
2. Overall survival
3. Response rate
4. Changes in tumour blood flow and vascular permeability (vascular permeability [Ktrans] and relative Cerebral Blood Volume [rCBV] values) during the first 20 days of treatment with bevacizumab in comparison with dexamethasone and the combination bevacizumab and 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

## **Overall study start date**

13/02/2007

## **Completion date**

01/02/2009

# **Eligibility**

## **Key inclusion criteria**

1. Patients present with histologically confirmed diagnosis of intracranial recurrent high grade glial tumour (World Health Organisation [WHO] grade IV). Patients may be entered based on local pathology from the original tumour specimen
2. Patients must have evidence of tumour progression following radiation and chemotherapy as measured by Magnetic Resonance Imaging (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:
  - 5.1. Adequate bone marrow reserve: Absolute Neutrophil Count (ANC) greater than  $1.5 \times 10^9/L$ , platelet count greater than  $100 \times 10^9/L$ , and haemoglobin greater than g/dL (6.21 mmol/L)
  - 5.2. Hepatic: total bilirubin less than two times the Upper Limit of Normal (ULN); Alkaline Phosphatase (ALP), Aspartate Transaminase (AST), and Alanine Transaminase (ALT) less than 3 x ULN
  - 5.3. Renal: serum creatinine less than 1.5 ULN
- These tests must be performed less than five days prior to enrolment. Eligibility for haemoglobin count may be reached by transfusion
6. Patients must have a Karnofsky Performance Score greater than 70%
7. Patients must be greater than 18 years of age, with a life expectancy of greater than eight 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 three months after discontinuation of study treatment. Women with childbearing potential must have a negative serum pregnancy test less than three days prior to study enrolment
10. Signed informed consent from the patient or legal representative is required

**Participant type(s)**

Patient

**Age group**

Not Specified

**Sex**

Both

**Target number of participants**

30

**Total final enrolment**

23

**Key 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 Anti-Epileptic Drugs). Patients must discontinue EIAEDs greater than 14 days prior to study enrolment. 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

**Date of first enrolment**

13/02/2007

**Date of final enrolment**

01/02/2009

## **Locations**

**Countries of recruitment**

Netherlands

**Study participating centre**

**Academic Medical Centre (AMC)**

Amsterdam

Netherlands

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## **Sponsor information**

**Organisation**

Academic Medical Centre (AMC) (The Netherlands)

**Sponsor details**

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**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.amc.uva.nl>

**ROR**

<https://ror.org/03t4gr691>

## **Funder(s)**

**Funder type**

Hospital/treatment centre

**Funder Name**

Academisch Medisch Centrum

**Alternative Name(s)**

Academic Medical Center, AMC

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Universities (academic only)

**Location**

Netherlands

## Results and Publications

**Publication and dissemination plan**

Not provided at time of registration

**Intention to publish date****Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Not provided at time of registration

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		01/08/2010	10/06/2021	Yes	No