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AVAstin and Temozolomide Attacking Relapsed glioma

Submission date	Recruitment status	[_] Prospectively registered
16/07/2007	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
16/07/2007	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
10/06/2021	Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
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

Study type(s)
Not Specified

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^2, 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(s)

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.

Key secondary outcome(s))
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

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 x 10^9/L, platelet count greater than 100 x 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

Healthy volunteers allowed
No

Age group
Not Specified

Sex
All

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
1100 DD

Sponsor information

Organisation
Academic Medical Centre (AMC) (The Netherlands)

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

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?
Results article		01/08/2010	10/06/2021	Yes	No