Bevacizumab, Radiotherapy and Temozolomide Safety study in biopsied or resected primary GBM patients

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Primary objective is determination of safety of combination of standard treatment with 3 bevacizumab infusions, followed by the standard adjuvant cycles of temozolomide. Secondary objectives: determination of: efficacy, classical response end-points...

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

Summary

ID

NL-OMON31960

Source
ToetsingOnline

Brief title
BERTES

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
Glioblastoma Multiforme, Malignant brain tumor

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, Glioblastoma, Radiotherapy, Temozolomide

Outcome measures

Primary outcome

Main parameter is safety, as scored by the NCI Common Toxicity Criteria Scale.

Secondary outcome

Other classical response end-points (PFS6, Time to Treatment Failure, OS12 and OS) will be combined with quality of life questionnaires (MMSE, QLQ-C30 v3.0 and EORTC BN-20) and compared to historical controls (Stupp data). All is monitored during the regularly scheduled outpatient clinic visits. The tumor MGMT status is determined in surgery specimens and will be used to study the predictive value for toxicity and clinical outcome.

Study description

Background summary

Median survival for patients with a newly diagnosed GBM is 12.1 months after resection of the tumor to the maximum extent, followed by 60 Gy irradiation in 30 x 2 Gy fractions. Maximal surgical resection is not feasible in a sub-group of patients due to the localization of their tumor, resulting in poorer prognosis. In a selected group of patients the median survival was 14.6 months when resection was followed by radiotherapy in combination with temozolomide during and thereafter temozolomide 6 monthly cycles. Chemoradiotherapy with temozolomide is the current standard treatment for GBM in our center. New combination treatments are required to lengthen survival of GBM patients. This trial utilizes the anti-edema effect of bevacizumab and its vascular normalization response to enhance the efficacy of chemoradiotherapy in resected and irresectable primary GBM patients.

Study objective

Primary objective is determination of safety of combination of standard

treatment with 3 bevacizumab infusions, followed by the standard adjuvant cycles of temozolomide. Secondary objectives: determination of: efficacy, classical response end-points, tumor imaging biomarkers and tissue samples biomarkers.

Study design

The study will employ a prospective observational study in one tertiary referral center for brain tumors in the Amsterdam area, the Netherlands, with multiple time measures.

Intervention

Study population will be treated with standard GBM chemoradiotherapy schedule plus additional 3 infusions of the angiogenesis inhibitor bevacizumab at a dose of 10 mg/kg during irradiation (e.g. one dose every 2 weeks during 6 weeks radiotherapy).

Study burden and risks

It is safe to add bevacizumab to the current practice of chemoradiotherapy in solid tumors, based on recent literature [Crane, 2006; Czito, 2007; Vredenburgh 2007] and preliminary results from a number of ongoing studies [Lai A et al, submitted; Gutin PH et al, submitted; Genentech, unpublished data]. In this study population we expect similar safety results as under standard chemoradiotherapy *Stupp regimen*. As estimated by power analysis, for n=20 this will imply 5 or less Grade 3/4 NCI toxicity events during chemoradiation and 10 or less Grade 3/4 NCI toxicity events during the entire treatment schedule.

Contacts

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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 with histologically proven GBM (biopsy or resection)
2. Can start 3-8 weeks post biopsy or surgery
3. Mini-Mental Status Score > 15
4. Karnofsky > 60
5. Adequate bone marrow function
6. Informed consent

Exclusion criteria

1. Age < 18 years
2. Pregnancy
3. Reluctance to use contraceptives
4. Inability to comply with protocol or study procedures (for example, an inability to swallow tablets)
5. Bleeding disorders
6. Anti-coagulant therapy
7. Prior chemotherapy or radiotherapy

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):	01-11-2007
Enrollment:	20
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:	Temodal
Generic name:	temozolomide
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	15-11-2007
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

ID: 27467
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2007-005644-24-NL
CCMO	NL20411.018.07
OMON	NL-OMON27467