Randomized trial assessing the significance of Bevacizumab in recurrent grade II and Grade III gliomas. The TAVAREC trial.

Published: 01-10-2010
Last updated: 04-05-2024

To explore if the addition of bevacizumab to temozolomide improves outcome as compared to treatment with temozolomide alone in patients with recurrent low grade and anaplastic glioma without combined 1p/19q co-deletion after prior radiotherapy and...

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

Summary

ID

NL-OMON43916

Source
ToetsingOnline

Brief title
TAVAREC

Condition

- Nervous system neoplasms malignant and unspecified NEC
- Nervous system neoplasms malignant and unspecified NEC

Synonym
recurrent anaplastic glioma, recurrent low grade glioma

Research involving
Human

Sponsors and support

Primary sponsor: European Organisation for Research in Treatment of Cancer (EORTC)
Source(s) of monetary or material Support: Hoffman la Roche,Hoffmann-La Roche

Intervention

Keyword: bevacizumab, glioma, recurrent, temozolomide

Outcome measures

Primary outcome

Overall survival at 12 months

Secondary outcome

Ovverall survival at 24 months, progression free survival: median, at 6 and at

12 months, time to neurocognitive progression, quality of life both in the

patient and his/her proxy, toxicity

Study description

Background summary

The prognosis of patient with recurrent low grade and anaplastic glioma without 1p/19q loss after radiotherapy and/or chemotherapy is dismal. most of these tumors recur as grade IV tumors, with a median survival after recurrence of about 12 months. Standard of care in that situation uisualy consists of treatment with temozolomide. This study aims to explore the the effect of the addition of a VEGF inhibitor, bevacizumab, to the treatment with temozolomide.

Study objective

To explore if the addition of bevacizumab to temozolomide improves outcome as compared to treatment with temozolomide alone in patients with recurrent low grade and anaplastic glioma without combined 1p/19q co-deletion after prior radiotherapy and or chemotherapy.

Study design

Randomized phase II study

Intervention

All patients will receive temozolomide chemotherapy which is considered standard of care in this disease. Patients randomized to the bevacizumab arm will receive intravenous bevacizumab once per two weeks until progression and as long this treatment is well tolerated.

Study burden and risks

The standard of care in this situation usually consists of treatment with temozolomide. To this treatment once every two weeks intravenous administration of bevacizumab is added. This treatment can be complicated by side effects. As part of the study treatment follow-up is somewhat more intensive, and quality of life questionaires have to be filled in by the patient and his/her proxy. In addition, neurocognitive evaluation is part of the study.

Contacts

Public
European Organisation for Research in Treatment of Cancer (EORTC)

Av E Mounier 89/11
Brussel B-1200
BE
Scientific
European Organisation for Research in Treatment of Cancer (EORTC)

Av E Mounier 89/11
Brussel B-1200
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Histologically proven grade II or grade III astrocytoma, oligodendroglioma or oligoastrocytoma according to the WHO 2007 at initial diagnosis.
- Demonstrated absence of 1p/19q co-deletion according to local diagnosis.
- Availability of biological material for central review processes and translational research projects
- First recurrence after initial treatment with either radiotherapy and/or chemotherapy.
- Enhancing recurrence on MRI scan.
- For non operated patients, recurrent disease must be at least one bi-dimensionally measurable contrast enhancing lesion with clearly defined margins by MRI scan, with minimal diameters of 10 mm, visible on 2 or more axial slices 5 mm apart, based on MRI scan done within two weeks prior to start of randomisation.
- Stable or decreasing dosage of steroids for 7 days prior to the baseline MRI scan.
No more than one line of chemotherapy (concurrent and adjuvant temozolomide chemotherapy is considered one line of chemotherapy)
- If given, chemotherapy must have consisted of either temozolomide or PCV, and patients must be off chemotherapy treatment for more than 6 months without progression.
- Patient may have undergone surgery for recurrence. If operated, residual and measurable disease after surgery is not required but histology must have confirmed the recurrence. Craniotomy or intracranial biopsy site must be adequately healed free of drainage or cellulitis, and the underlying cranioplasty must appear intact at the time of randomisation.
- Absence of known hypersensitivity to any part of the Bevacizumab or Temozolomide formulations, to Chinese hamster ovary cell products or other recombinant human or humanized antibody.
- Normal hematological, renal and hepatic function functions
- Urine dipstick for proteinuria < 2+.
- Age * 18 years
- WHO Performance status 0 - 2
- Women of child bearing potential must have a negative serum or urine pregnancy test
- Female patients within one year of entering the menopause as well as males must agree to use an effective non-hormonal method of contraception during the treatment period and for at least 6 months after the last study treatment.
- Female should not be breast feeding
- Absence of any psychological, familial, sociological or geographical factors potentially hampering compliance with the study protocol and follow-up schedule
- written informed consent

Exclusion criteria

- Radiotherapy within the three months prior to the diagnosis of progression
- Radiotherapy with a dose over 65 Gy, stereotactic radiosurgery or brachytherapy unless the

recurrence is histologically proven
- Current or recent (within 4 weeks before randomization) treatment with another investigational drug
- Prior treatment with Bevacizumab or other VEGF inhibitors or VEGF-Receptor signaling inhibitors
- Invasive procedures (surgical resection, open biopsy, significant traumatic injury or any other major surgery involving entry into a body cavity) within 4 weeks prior to randomization, or anticipation of the need for major surgery during the course of the study treatment.
- Core biopsy (excluding intracranial biopsy) or other minor surgical procedure within 7 days prior to randomization.
- Previous other malignancies, except for any previous malignancy which was treated with curative intent more than 5 years prior to randomisation, and except for adequately controlled limited basal cell carcinoma of the skin, squamous carcinoma of the skin or carcinoma in situ of the cervix
- Any significant cardiovascular disorder
- Inadequately controlled hypertension (defined as systolic blood pressure >150 mmHg and/or diastolic blood pressure >100 m Hg)
- Any thrombotic or hemorrhagic event, including arterial or venous thrombosis * 12 months prior to randomization
- Current or recent (within 10 days of first dose of Bevacizumab) use of aspirin (> 325 mg/day) or other NSAID with anti-platelet activity or treatment with dipyramidole, ticlopidine, clopidogrel or cilostaz.
- International normalized ratio (INR) > 1.5 ULN and activated partial thromboplastin time (aPTT) >1.5 × the ULN.
- Use of full-dose anticoagulants at baseline (but prevention of thrombosis with low-dose anticoagulant is allowed)

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-02-2011
Enrollment:	46
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Avastin
Generic name:	bevacizumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	temozolomide
Generic name:	temodar
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	01-10-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-12-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-09-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	09-07-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-01-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-03-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-06-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-10-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-12-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-09-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-11-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

(Rotterdam)

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	EUCTR2009-017422-39-NL
ClinicalTrials.gov	NCT01164189
CCMO	NL33733.078.10