Phase III trial comparing conventional adjuvant Temozolomide with dose-intensive Temozolomide in patients with newly diagnosed glioblastoma

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To determine if dose-intensifying the adjuvant temozolomide component of the chemoradiation treatment enhances treatment efficacy as measured by overall survival.

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

Summary

ID

NL-OMON31602

Source
ToetsingOnline

Brief title
RTOG 0525 / EORTC 26052-22053

Condition

- Nervous system neoplasms malignant and unspecified NEC
- Nervous system neoplasms malignant and unspecified NEC
- Nervous system, skull and spine therapeutic procedures

Synonym
braintumour, Glioblastoma

Research involving
Human

Sponsors and support

Primary sponsor: European Organisation for Research in Treatment of Cancer (EORTC)
Source(s) of monetary or material Support: EORTC,Schering-Plough

Intervention

Keyword: Adjuvant, Dose intensification, Glioblastoma, Temozolomide

Outcome measures

Primary outcome

To determine if dose-intensifying the adjuvant temozolomide component of the chemoradiation treatment enhances treatment efficacy as measured by overall survival.

Secondary outcome

1. To validate the association between tumor MGMT gene promotr methylation status and treatment response.

2. To determine if dose-intensifying the adjuvant temozolomide component of the chemoradiation treatment enhances treatment efficacy as measured by progression-free survival.

3. To determine in patients with unmethylated MGMT if dose-intensifying the adjuvant temozolomide component of the chemoradiation treatment enhances treatment efficacy (overall and progression-free survival) compared with patients receiving conventional temozolomide dosing.

4.To determine in patients with methylated MGMT if dose-intensifying the adjuvant temozolomide component of the chemoradiation treatment enhances treatment efficacy overall and progression-free survival) compared with patients receiving conventional temozolomide dosing.

5. To compare and record the toxicities of the conventional and dose-intense

chemotherapy regims.

6. To evaluate wether 6-month progression-free survival is associated with

overall survival.

Study description

Background summary

The prognosis of patients with glioblastoma multiforme is poor. Chemotherapy with temozolomide improves, when administered concomitant and adjuvant, the treatmentresult of radiotherapy. Dose-intensification of chemotherapy may further improve the treatment outcome.

Study objective

To determine if dose-intensifying the adjuvant temozolomide component of the chemoradiation treatment enhances treatment efficacy as measured by overall survival.

Study design

Phase III randomised, open intervention study.

Intervention

In both treatmentarms patients will have radiation of the primary tumour area (60 Gy in 2 Gy fractions) combined with daily temozolomide (75 mg/m2) , during maximum 49 days, followed by adjuvant chemotherapy:

* Conventional arm: Temozolomide 150 - 200 mg/m2 for 5 consecutive days of a 28-day cyclus. Duration: 6 - 12 cycli
* Experimental arm: Temozolomide 75-100 mg/m2 for 21 consecutive days in a 28-day cyclus. Duration 6 - 12 cylci.

Study burden and risks

The extra burden constists of a maximum of 24 venous punctions in the period of the adjuvant chemotherapy and pregnancy test before treatment. At the start of this study dose-intensification, according to the information known at that the

moment, has demonstrated to be safe without extra complications.
After the review in June 2007 the studycoördinators had to conclude that the risk known for temozolomide could be more likely to occur due to the dose-dense schedule or worse if the event did occur.

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. Histopathologically proven diagnosis of glioblastoma. Since gliosarcoma is a variant of glioblastoma, gliosarcoma is an eligible diagnosis.
2. Patients must have at least 1 block of tissues available for analysis of MGMT status.
3. Diagnosis must be made by open surgical biopsy or excision.
4. The tumor must have supratentorial component.
5. Patients must have recovered from the effects of surgery, post-operative infection, and

other complications before study registration.
6. A diagnostic cotnrast-enhanced MRI (or CT-scan if MRI is not available) of the brain preoperatively and postoperatively prior to the initiation of radiotherapy, within 28 days prior to study registration.
7. Therapy must begin within 5 weeks after surgery.
8. Karnofsky performance status more or equal then 60.
9. Age >= 18 years.

Exclusion criteria

1. Prior invasive malignacy unless disease free for more then 3 years.
2. Recurrent or multifocal malignant gliomas.
3. Histopathologically diagnosis made only by stereotactic biopsy.
4. Metastases detected below the tentorium or beyond the cranial vault.
5. Prior chemotherapy or radiosensitizers for cancers of the head and neck region.
65. Prior radiotherapy to the head or neck, resulting in overlap of radiation fields.
7. Severe, active co-morbidity:
* Unstrable angina and/or congestive heart failure requiring hospitalization.
* Transmural myocardial infarction within the last 6 months.
* COPD exacerbation or other respiratory illness requiring hospitalization or precluding study therapy at the time of registration.
* Hepatic insufficiency resulting in clinical jaundices and/or coagulation defects.
* Acquired Immune Deficiency Syndrome based upon current CDC definition; HIV testing is not required.
* Major illnesses or psychiatric impairments that in the investigator's opinion will prevent adminstiration or completion of protocol therapy.
* Active connectieve tissue disorders, such as lupus or scleroderma, that in the opinion of the treating physician may put the patients at high risk for radiaton toxicity.
8. Women of childbearing potrential and men who are secually active and not willing/able to use medically acceptabel forms of contraception.
9. Pregnant or lactating women, due to possible adverse effects on the developing fetus or infant due to study drug.
10. Prior allergic reaction to temozolomide.

Study design

Design

Study phase:	3
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):	13-06-2008
Enrollment:	100
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Temodar
Generic name:	Temozolomide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	09-01-2007
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-06-2007
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-10-2007
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-03-2008
Application type:	Amendment

Review commission: METC Brabant (Tilburg)

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	EUCTR2005-005177-29-NL
ClinicalTrials.gov	NCT00304031
CCMO	NL13696.028.06