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

Published: 24-11-2006 Last updated: 10-05-2024

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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Scientific

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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
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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

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