A Phase II Study of Concurrent Radiation and Temozolomide Followed by Temozolomide and Lomustine (CCNU) in the Treatment of Children with High Grade Glioma

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Determine whether temozolomide given during radiation therapy followed by the combination of temozolomide and CCNU as adjuvant therapy results in an improvement in event-free survival compared to historical control cohorts.To further assess the...

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

Summary

ID

NL-OMON30368

Source
ToetsingOnline

Brief title
Temozolomide and Lomustine for children with a high grade glioma

Condition

- Nervous system neoplasms malignant and unspecified NEC
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Synonym
High Grade Glioma; malignant Brain tumor

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Kinderoncologie Nederland
Source(s) of monetary or material Support: Ministerie van OC&W,Kosten van de zorg en mediactie worden vergoed door de zorgverzekeraar; Kosten van data management en van biologisch onderzoek door de COG

Intervention

Keyword: children, high grade glioma, phase II, Temozolomide

Outcome measures

Primary outcome

Event Free Survival of patients compared to historical control cohorts.

Toxicity measured according to standard scores.

Secondary outcome

Not applicable

Study description

Background summary

Children with high grade glioma continue to have a poor prognosis, despite the use of multimodality therapy including surgery, radiation therapy and chemotherapy. Complete resection is of prognostic significance, but rarely possible and surgery alone is rarely curative. Radiation prolongs survival time but has a limited impact on long-term overall survival. The role of chemotherapy is not yet clear.
The SKION committee for high grade glioma studied the open research protocols and choose to participipate in the COG ACNS 0423 protocol. Except for scientific reasons we also wanted to avoid that patients with a poor prognosis are exposed to a protocol with too much burden or risks. According to the committees judgement the ACNS 0423 has a optimal balance between expected burden and toxicity on one hand and efficacy on the other hand.
The ratio behind this protocol is the expected synergistic effect from the combination of Temozolomide and CCNU. Temozolomide, an oral alkylating agent, has shown significant pre-clinical and clinical activity against high grade gliomas and is well tolerated by children. Nitrosurea are considered amongst the most active agents against high grade gliomas. The activity of Temozolomide

is influenced by the amount of MGMT: an enzyme that repairs Temozolomide induced DNA damage, and therefore induces resistance. High grade gliomas in children seem to respond less to Temozolomide than high grade gliomas in adults. A possible explanation for this could be a difference in the amount of MGMT. Nitrosurea deplete the cel of MGMT. The synergistic effect of Temozolomide and BCNU has been shown in mice with human tumor xenografts and has been studied in adults with high grade gliomas. In a recent phase I study in children with newly diagnosed high grade glioma the MTD for the combination of Temozolomide and CCNU has been determinded. (The advantage of CCNU compared to BCNU is its excellent oral bioavailalibility and less pulmonary toxicity) (see also attached safety report).

Study objective

Determine whether temozolomide given during radiation therapy followed by the combination of temozolomide and CCNU as adjuvant therapy results in an improvement in event-free survival compared to historical control cohorts.
To further assess the toxicity of adjuvant treatment with CCNU and temozolomide following XRT and concurrent temozolomide in a larger group of patients.
Biological studies amongst others to explore mechanisms of resistance.

Study design

A single arm phase II study in which children with high grade gliomas receive after surgery simultaneous radiation therapy and temozolomide during for 42 days (90mg/m2/d). Four weeks following the completion of radiotherapy the patient will receive a maintenance therapy with the combination of temozolomide (160 mg/m2/d x 5 days) and CCNU (90 mg/m2/d on day 1 of the temozolomide) each 42 days for a total of 6 cycles

Intervention

See study design

Study burden and risks

The additional burden and risks for the participants are the result of the addition of the chemotherapy given in this protocol compared to the standard treatment with surgery and radiation therapy. The chemotherapy can be taken at home, orally, which means a minimal extra burden. The side effects of chemotherapy may differ per patient. In general and as far as known the side effects of temozolomide and CCNU separately, in combination and on short term are looked upon as relatively mild. The long term side effects are not yet fully known.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Cildren between 3 and 22 years of age, with a biopsy proven, newly diagnosed high grade glioma (anaplastic astrocytoma; glioblastoma multiforme; gliosarcoma) of the brain or spinal cord.

Exclusion criteria

Primary high grade glioma of the brain stem; proved metastases; Karnofsky performance score < 50% for children > 16 years of age and Lansky < 50 for children = / < 16 years of

age; life expectancy < 8 weeks; prior treatment other than surgery and corticosteroids

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):	01-12-2006
Enrollment:	8
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO

Date:	30-10-2006
Application type:	First submission

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2006-005077-21-NL
CCMO	NL14455.091.06