Combination therapy for children with malignant pontine gliomas.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28201

Source
Nationaal Trial Register

Brief title
DIPG study, VUmc 01

Health condition

Diffuse intrinsic pontine glioma
Malignant pontine glioma

Sponsors and support

Primary sponsor: VU University Medical Center
Source(s) of monetary or material Support: VONK (VUmc research into childhood cancer)
Stichting Semmy (Semmy Foundation)

Intervention

Outcome measures

Primary outcome

Phase a: Tolerability of gemcitabine at 3 dose levels (toxicity according to CTCAE-4);

Phase b: Tolerability of erlotinib and everolimus at two dose levels when added to bevacizumab-irinotecan (toxicity according to CTCAE-4);

Phase c: Median overall survival.

Secondary outcome

Phase a: Clinical response rate, response rate on MRI according to the WHO-criteria and the median progression free survival;

Phase b: Median overall survival from time of progression;

Phase c: Quality of life based on standardised questionairres.

Study description

Background summary

Children with malignant pontine gliomas have a dismal prognosis. The median overall survival is approximately nine months, the two-year survival rate less than 10%. In the past twenty years the prognosis has remained unchanged, despite several treatment strategies. In this study, the efficacy and feasibility of the radiosensitizer gemcitabine and a new combination of targeted agents will be investigated in three phases. Depending on the maturation of the present study, and on preceding therapy, an individual patient may enrol in phase a, phase a and b, or in phase c. Patients are separately asked informed consent for a biopsy: apart from histological confirmation, the tissue will also be used for retrospective correlation of DNA/RNA amplification or mutation and protein expression and clinical response.

Study objective

Combination therapy consisting of cytotoxic drugs and multitargeted therapy is needed to improve the dismal prognosis of the multiresistant malignant pontine gliomas.

Study design

N/A

Intervention

At diagnosis: If informed consent is obtained, a biopsy will be performed.

Phase a (after diagnosis):

Cohorts of 3 patients will receive local radiotherapy (54Gy) with 3 escalating dose levels of gemcitabine, or until the MTD has been established. The starting dose (140 mg/m2) is 80% of the MTD in adults with GBM.

Phase b (at disease progression):

Backbone therapy consists of irinotecan 125 mg/m2 IV 2-weekly and bevacizumab 10 mg/kg IV 2-weekly. Cohorts of 3 patients will receive 2 escalating dose levels of erlotinib, or until MTD has been established. If no DLT occurs during the first two courses, patients will be treated in an expanded cohort on the same dose level, until progressive disease or death occurs. The starting dose of erlotinib (65 mg/m2/day) is 80% of the MTD established in combination with temozolomide in children.

After the MTD of erlotinib has been established, everolimus is added to bevacizumab, irinotecan and erlotinib. Cohorts of 3 patients will receive 2 escalating dose levels of everolimus, or until MTD has been established. If no DLT occurs during the first two courses, patients will be treated in an expanded cohort on the same dose level, until progressive disease or death occurs.The starting dose (4 mg/m2) is 80% of the MTD in children.

Phase c (after diagnosis):

If radiosensitizer gemcitabine is feasible in combination with radiotherapy in Phase a, and concurrent treatment with irinotecan, bevacizumab, erlotinib and everolimus is feasible in Phase b, newly diagnosed patients in Phase c will receive both treatments subsequently, with a 2-week interval and drugs dosed at the established MTD’s.

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Eligibility criteria

Inclusion criteria

1. Newly diagnosed DIPG;

2. Newly diagnosed unresectable grade II-IV pontine glioma;

3. Age between 3 years and 18 years;

4. Willingness to perform a pregnancy test in females of child bearing age;

5. Written informed consent;

6. Platelet count ≥ 75 x109/L (transfusion independent);

7. Peripheral absolute neutrophil count (ANC) ≥ 0,75 x109/L;

8. Direct bilirubin ≤ 1.5 x upper limit of normal (ULN) for age;

9. SGPT (ALAT) < 5 x upper limit of normal (ULN) for age;

10. Serum creatinine ≤ 1.5 x upper limit of normal (ULN) for age;

11. Performance status (Lansky or Karnofsky score) ≥ 40%.

Exclusion criteria

1. Pilocytic (grade 1) astrocytomas;

2. Presence of diffuse leptomeningeal disease;

3. Patients having been pre-treated for DIPG;

4. Pregnant or breastfeeding;

5. Other contra-indications for chemotherapy;

6. Clinically no neurofibromatosis type 1 (NF-1).

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2011
Enrollment:	16
Type:	Anticipated

Ethics review

Positive opinion

Date:	24-06-2010
Application type:	First submission

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
NTR-new	NL2265
NTR-old	NTR2391
Other	VUmc METc : 2010/164 pro09/96
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A