A study of Carboplatin with radiotherapy and Isotretinoin in patients with other than average risk medulloblastoma/PNET.

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The goal of this study is to determine whether radiosensitization with carboplatin or the addition of Isotretinoin to maintenance therapy improves cure rates for children with other than average risk medulloblastoma/PNET.

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON21835

Bron
NTR

Verkorte titel
ACNS0332

Aandoening

brain tumor, medulloblastoma

Ondersteuning

Primaire sponsor: International: Children's Oncology Group (COG)
Netherlands: Dutch Childhood Oncology Group (DCOG)
Childhood Oncology Group (COG)
COG Operations Center
440 E. Huntington Drive, 4th Floor
Arcadia, CA 91006-3776
USA
Tel: (626) 447-0064

Overige ondersteuning: DCOG

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

1. Long term event-free survival for high risk
medulloblastoma/PNET patients after carboplatin radiosensitization;
2. Long term event-free survival for high risk
medulloblastoma/PNET patients after Isotretinoin.

Toelichting onderzoek

Achtergrond van het onderzoek

Medulloblastoma/PNET is the most common malignant childhood brain cancer. The goal of this study is
to determine whether radiosensitization with carboplatin or the addition of Isotretinoin to maintenance
therapy improves cure rates for children with other than average risk medulloblastoma/PNET. All
patients will receive standard therapy consisting of surgery, radiation therapy and chemotherapy. Subsets
of patients will be randomly assigned to receive carboplatin radiosensitization, Isotretinoin during
maintenance, both, or neither. Carboplatin has activity as a single agent against medulloblastoma and it
has been shown to enhance radiation-induced tumor cell kill. A previous study, CCG-99701, demonstrated that it was feasible and safe to administer carboplatin on a daily basis during radiation
therapy. Laboratory-based studies have shown that Isotretinoin effectively kills patient-derived
medulloblastoma cells ex vivo and in animal models of medulloblastoma. Furthermore, this agent acts
synergistically with cisplatin in vitro and in animal models. Isotretinoin has previously been safely
administered to neuroblastoma patients at the same dose planned for this study. Correlative biology
studies are incorporated into the research design.

Doel van het onderzoek

The goal of this study is to determine whether radiosensitization with carboplatin or the addition of Isotretinoin to maintenance therapy improves cure rates for children with other than average risk medulloblastoma/PNET.

Onderzoeksopzet

The primary endpoint for the evaluation of treatment efficacy will be time to an event, which will be used to compute the event-free survival (EFS) percentage. An event comprises disease progression or recurrence, occurrence of a second malignant neoplasm, or death from any cause. Secondary endpoints in this analysis will be tumor response to radiation therapy ± carboplatin, and time to death, from which the survival (S) percentage will be computed.

Onderzoeksproduct en/of interventie

Following neurosurgical procedure and staging, patients will be randomized to receive either 36 Gy craniospinal irradiation with appropriate boost to the tumor bed or the same radiation regimen with addition of carboplatin as a radiosensitizing agent. All patients must begin therapy within 31 days of surgery. The dose of carboplatin will be 35 mg/m2/day for 30 doses over 6 ½ weeks. All patients will receive vincristine 1.5 mg/m2 once per week during radiation therapy for a total of 6 doses.

Following radiation and a 6 week rest period, patients will then undergo Maintenance chemotherapy with cisplatin, vincristine, and cyclophosphamide in 28 day cycles for a total of 6 cycles. Note: Maintenance may be delayed up to 8 weeks.

Approximately 10% of patients will drop counts between 4-6 weeks after completing radiation therapy and Maintenance should not be initated until counts recover.
Patients will be randomized to receive either Isotretinoin during Maintenance or no additional drug.

Patients randomized to Isotretinoin will receive 80 mg/m2 twice daily on Day 1 and Days 16-28 in 28 day intervals during Maintenance and Days 15-28 during Continuation Therapy for a total of 12 cycles beginning concurrently with Maintenance chemotherapy and continuing for approximately six months after completion of chemotherapy.

Contactpersonen

Publiek

Prinses Máxima Centrum voor kinderoncologie
Carin Damen-Korbijn
Den Haag 2545 CJ

The Netherlands
088 972 7272

Wetenschappelijk

Prinses Máxima Centrum voor kinderoncologie
Carin Damen-Korbijn
Den Haag 2545 CJ
The Netherlands
088 972 7272

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age greater than or equal to 3 and less than 22 years at the time of diagnosis;

2. Newly diagnosed, previously untreated: (1) M0 Medulloblastoma with >1.5 cm2 residual; (2) M+ Medulloblastoma; (3) M0 or M+ Supratentorial PNET (including pineoblastoma). Patients with diffusely anaplastic medulloblastoma are eligible regardless of M-stage or residual tumor. All patients with M4 disease are not eligible;

2. A pre-operative MRI scan of the brain with and without contrast is required;

3. Lumbar CSF cytology examination must be obtained pre-operatively or within 31 days following surgery;

4. Patients must have a Karnofsky performance level of ≥ 30 for patients > 16 years of age or a Lansky performance scale of ≥ 30 for patients ≤ 16 years of age and life expectancy > 8 weeks;

5. No previous chemotherapy or radiation therapy;

6. Patients taking Accutane (Isotretinoin) for acne must discontinue drug use with this indication prior to enrollment. Corticosteroids should not be used during chemotherapy administration as an antiemetic because of their effect on the blood-brain barrier;

7. The use of strong CYP450 3A4 inhibitors and inducers should be avoided with vincristine and cyclophosphamide;

8. CISplatin should be used with caution with nephrotoxic drug. Patients receiving potentially ototoxic drugs should be closely monitored for signs of ototoxicity;

9. No other experimental therapy is permitted while on study;

10. Adequate renal function;

11. Adequate liver function;

12. Adequate bone marrow function;

13. Female patients who are post-menarchal must have a negative pregnancy test. Lactating female patients must agree not to breast-feed while on this trial. Males or females of reproductive potential may not participate unless they have agreed to use an effective contraceptive method;

14. All patients and/or their parents or legal guardians must sign a written informed consent;

15. All institutional, FDA, and NCI requirements for human studies must be met.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

See general (inclusion) criteria.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Factorieel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	06-04-2011
Aantal proefpersonen:	8
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Ethische beoordeling

Positief advies

Datum:	13-03-2012
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 41634
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3196
NTR-old	NTR3347
CCMO	NL29915.091.09
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON41634

Resultaten

Samenvatting resultaten
N/A