ACNS0332: Efficacy of Carboplatin Administered Concomitantly With Radiation and Isotretinoin as a Pro-Apoptotic Agent in Other Than Average Risk Medulloblastoma/PNET Patients - A Groupwide Phase III Study

Published: 19-08-2010
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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.

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

Summary

ID

NL-OMON41634

Source
ToetsingOnline

Brief title
Carboplatin and isotretinoin for children with high risk medulloblastoma

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
medulloblastoma, pnet; 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,NCI grant/vergoeding door COG (inmiddels komen te vervallen)

Intervention

Keyword: carboplatin/isotretinoin, children, high-risk medulloblastoma/PNET, phase III randomized

Outcome measures

Primary outcome

To determine whether carboplatin radiosensitization increases long term

event-free survival for high risk

medulloblastoma/PNET patients.

To determine whether Isotretinoin increases long term event-free survival for

high risk

medulloblastoma/PNET patients.

Secondary outcome

To compare residual disease response to radiation alone versus radiation plus

carboplatin.

To identify molecular prognostic indicators suitable for patient stratification

in future trials.

Study description

Background summary

Medulloblastoma is the most common malignant childhood brain cancer. Standard treatment for children with other than average risk medulloblastoma consists of surgery, followed by radiation therapy and chemotherapy. The goal of this study is
to determine whether radiosensitization with the addition of carboplatin during radiation therapy improves the poor cure rates (50-60%) for children with other than average risk medulloblastoma.

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.

Patients will be randomly assigned to receive carboplatin radiosensitization or not. Primary outcome measurement will be eventfree survival.

This protocol previously included a randomization to 4 study arms, two of which (arm C and C with the addition of Isotretinoin in maintenance treatment) have been closed now (amendment 3). Arm A and B remain open to answer the question whether the addition of carboplatin during radiotherapy will lead to a beter event free survival,
This protocol also previously included supratentorial primative neuroectodermal tumor (PNET) patients in addition to medulloblastoma patients. The PNET component of the trial has concluded due to new insights regarding molecular biology. This tumor is so much different from medulloblastoma that heterogeneity of tretment effects across tumor types may recude power. The study has been re-powered allowing additional inclusion of 100 patients (amendment 2).

Study objective

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.

Study design

This is a mulitcenter phase III randomized factorial-designed open study. All patients will be randomised to receive radiation therapy with or without carboplatine and chemotherapy with or without the addition of isotretionoine

during the maintenance fase. The study arms with isotretinoine have already been closed as per 01/27/2015 (amendment 3).

Intervention

Treatment comparisons will be made between induction radiation therapy alone to radiation therapy and carboplatin, both followed with maintenance therapy with or without isotretinoin.

Study burden and risks

The risks that are associated with this study involve the potential side effects of the administration of carboplatin during radiotherapy.
The risks that were associated with the addition of isotretinoin to consolidation/maintenance therapy are not applicable anymore, i.e. after the second randomisation being closed.
Also the extra burden for study participants involving a longer treatment duration (24 weeks longer) for patients treated with isotretinoine during maintenance phase, does no longer apply.

The risks and burden involved with this treatment are justified by (1) the overall goal to improve event free survival of high-risk medulloblastoma; (2) the proved safety of the drug doses used in this trial; and (3) adequate monitoring of study subjects during and after treatment

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

Age greater or equal to 3 y and less than 22 y at time of diagnosis
Newly diagnosed previously untreated medulloblastoma (M0 with >1.5 cm2 residual, or M1-3); (amendment 2: inclusion sPNET discontinued)
Written informed consent (parents and patient)

Exclusion criteria

Age less than 3 y
Extraneural metastases
Karnofski/Lansky < 50% and life expectancy <= 8 weeks
Inadequate organ function prior to start of therapy (renal, liver, bonemarrow)
Previous chemotherapy or radiation therapy
Other experimental therapy

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:	Recruiting
Start date (anticipated):	15-06-2011
Enrollment:	21
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Accutane a.o.
Generic name:	isotretinoin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Cytoxan
Generic name:	cyclophosphamide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Oncovin
Generic name:	vincristinsulphate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Paraplatin
Generic name:	carboplatin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Platinol
Generic name:	cisplatin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	19-08-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-01-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-10-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-11-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-08-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-09-2015
Application type:	Amendment
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

ID: 21835
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2009-016059-23-NL
ClinicalTrials.gov	NCT00392327
CCMO	NL29915.091.09
OMON	NL-OMON21835