Phase II single-arm studies of gemcitabine in combination with oxaliplatin in refractory and relapsed pediatric solid tumors

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To assess the response rate to the combination of gemcitabin plus oxlaiplatin in 5 different strata of relapsed/refractory pediatric solid tumors, in whom standard treatment has failed. Secondary objectives are the safety, the duration of response,...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON29764

Source
ToetsingOnline

Brief title
ITCC-GemOx study

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
solid tumors in children

Research involving
Human

Sponsors and support

Primary sponsor: Institue Goustave Roussy
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: children, gemcitabine, oxaliplatin, solid tumors

Outcome measures

Primary outcome

To assess teh objectiev response rate in children with relapsed/refractory

solid tumors in whom standard treatment has failed.

The response rate will be assessed per startum, and the study includes 5

different strata:

- medulloblastoma

- neuroblasoma

- osteosarcoma

- miscelleneous slid tmors (non-brain)

- miscelleneous brain tumors.

Secondary outcome

Secondary objectives are the safety, the duration of response, the time to

progression and survival, and the value of PET-scans in the response evaluation

of osteosarcoma.

Study description

Background summary

Pediatric tumors are rare and can be divided in hematlogical malignancies and

solid tumors. In the Netherlands approximately 280 children per year are diagnosed with a solid tumor. Solid tumors are very heterogeneous and consist of many small subgroups (less than 20 new patients per year). The overall cure rate is approximately 70%. In soem subrgoups, such as stage 4 neuroblastoma or pontine glioma, prognosis is much worse, and cancer is still the leading cause of death due to disease in children. Therefore, we urgently need new drugs to improve the prognosis.
In this study we aim at assessing the response rate to a combination of gemcitabin and oxaliplatin in children with relapsed/refractory solid tumors who have failed standard treatment. Five different strata will be included: neuroblastoma, osteosarcoma, medulloblastoma, other brain tumors and other solid non-brain tumors. For the first 2 cohorts some activity was seen in phase I studies (oxaliplatin, see the protocol). Medulloblastoma is included because it is in general the most chemo-sensitive brain tumor. The other 2 groups aim at screening efficacy in a larger group of children, and are descrptive in nature.
Gemcitabien showed limited activity in phase I studie sin children, but in-vitro synergy with oxaliplatin has been dmeonstrated, and this drug is an anti-metabolite, which are currently not available to childen with solid tumors. Given its activity in adults (althuogh in carcinomas which are rare in children) we feel thsi warrants further clinical investigation. Oxaliplatin did show some activity in phase I studies, is not cross-resistant with cisplatin, en has a different toxicty profile when compared with cisplatin (no auditory or renal toxicity).
A 2-weekly schedule was chosen as it is patient friednly and it may caus eless hematological toxiicty. Both drugs can be combined full-dose in adult studies, and there are no differences in PK between adults and children. Because of teh risk of peripheral neuropathy with oxaliplatin currently 12 courses are planned, however, in case of individual benefit more courses may be given.

Study objective

To assess the response rate to the combination of gemcitabin plus oxlaiplatin in 5 different strata of relapsed/refractory pediatric solid tumors, in whom standard treatment has failed. Secondary objectives are the safety, the duration of response, the time to progression and survival, and the value of PET-scans in the response evaluation of osteosarcoma.

Study design

This multi-center study will be performed with the ITCC-consortium, with 32 centra in several European countries. It si a single-arm study with 29 subjects pe arm at maximum. Only in the miscelleneous solid tumor arm 40 patienst may be included. A 2-stage design is used, hence if no responses occur in the first 9-12 patients (see the protocol for statistical details) an arm may be closed.

Intervention

Treatment consists of 12 courses of GemOx (or more in case of individual benefit), which consists of gemcitabine 1000 mg/m2 IV in 100 minutes followed by oxaliplatin 100 mg/m2 IV in 120 minutes on one day, every 14 days. This infusions can be given at the day-care unit.

Study burden and risks

Treatment consists of 12 days of chemotherapy administration at the day-care unit over a 6-months treatmnet period. Additional visits to the hospital may be needed for tumor evaluation.

At inclusion we will perform physical examination, tumor-evaluation (scans), blood tests and a pregnancy test for females with child-bearing potential.
During treatment pateints will have regular blood sampling, and will experience general side-effects from chemotherapy such as hair loss, nausea and vomiting. cytopenia, and possibly peripheral neuropathy.
Follow-up tumor evaluations are needed.

For patients with osteosarcoma a tumor biopsy may be necessary. There is a separate question in this patient group regarding the value of PET-scans for response evaluation.

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

- relapsed or refractory pediatric solid tumors
- age 6 months up to 21 years
- measurable primary and/or metastatic disease
- no more than 1 salvage therapy for relapse
- Lansky play score over 60 or ECOG 1
- adequate organ function
- life expectancy > 3 months
- wash out or prior therapy of 3 weeks
- written informed consent

Exclusion criteria

- Other antitumor therapy
- pre-existing sensory or motor neuropathy >grade 2 (except when caused by tumor)
- allergic reaction to platinum compounds
- symptomatic brain metastases

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-04-2007
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Eloxatin
Generic name:	oxaliplatin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Gemzar
Generic name:	gemcitabin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	23-01-2007
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-07-2007
Application type:	Amendment
Approved WMO Date:	27-08-2007
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2006-001065-41-NL
CCMO	NL13638.078.06