# A phase II study of the combination of gemcitabine with 131I-MIBG therapy for children with neuroblastoma without other treatment options.

No registrations found.

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

## Summary

### ID

NL-OMON24917

**Source**
NTR

**Brief title**
MIBG-Gem

**Health condition**

neuroblastoma, children, relapsed, progressive

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum Amsterdam
**Source(s) of monetary or material Support:** Stichting Kinderen Kankervrij Nederland

### Intervention

### Outcome measures

**Primary outcome**

Determination of efficacy as measured by response rate (and time-to-event measurements).

### Secondary outcome

Characterization of safety and toxicity profile.

## Study description

### Background summary

Pediatric tumors are rare and neuroblastoma accounts for 10% of all childhood cancers. Neuroblastoma can present in different stages, stage IV in patients older than 1 year of age represents the most frequent form. This stage is diagnosed in the Netherlands in 25 patients per year. The overall cure rate for childhood cancer with current treatment protocols is approximately 70%, but cancer is still the leading cause of death due to disease in children. Despite intensive treatment for neuroblastoma stage IV disease cure rate is far worse: a 5-year survival rate of only 30-40%. Therefore, we urgently need new drugs to improve prognosis. In this study we aim at assessing the efficacy and toxicity of the combination of gemcitabine and 131I-MIBG in children with relapsed or progressive neuroblastoma. Children will be divided in 2 strata: MIBG pretreated and MIBG-naive. Gemcitabine is a type of drug (anti-metabolite) which is currently not available in the treatment protocols. Its activity is extensively shown in solid tumours in adults. Furthermore, since gemcitabine has a radiosensitizing effect, it is part of the combination treatment with external beam radiotherapy in the treatment of some adult tumours. Extensively preclinical evidence has proven that gemcitabine as a single drug is quite effective in neuroblastoma cell lines. In phase I studies with gemcitabine in children, a mild toxicity profile was seen. The maximum tolerated dose (MTD) of gemcitabine single agent in children with solid tumors is 1200 mg/m2/dose (3 weeks, 1 weeks rest). The dosages at which gemcitabine shows radiosensitizing effect are much lower than the MTD. In this study, we will use a startdose of gemcitabine of 375 mg/m2/ dose.
131I-MIBG single agent has shown its efficacy in patients with neuroblastoma both in upfront and in relapse setting with response rates in relapse setting of 10-43%. Given the radiosensitising effect and the mild toxicity profile we feel the combination of gemcitabine and 131I-MIBG warrants further clinical investigation.

This multi-center study will be performed in collaboration with German Pediatric Oncology Hematology Group (GPOH) in 10-12 diffenrent centres in the Netherlands and Germany. It is a single-arm study according to a 2-stage design with stopping rules for efficacy and toxicity. We start with a dose of 375 mg/m2/dose of gemcitabine. When 6 patients have been treated at the first dose-level a safety analysis will be performed. If dose-limiting toxicity is encountered in 2 or more patients, the trial stops. Otherwise, enrolment will be continued until 19 patients have been treated. Then an interim analysis will be performed after which, in case of intermediate reponse and no severe toxicity, study will be continued with an escalated dose (500 mg/m2). If response rates are very high at interim analysis and there's

limited toxicity, enrollment will be continued at the same dose of gemcitabine (375 mg/m2) up to 47 patients. If study is continued at the escalated dose level, another safety analysis will be performed after treating the first 6 patients and an interim analysis will be perfomed after 19 patients at that dose. Patient numbers will be balanced per stratum based on previous MIBG-treatment, enrollment will be continued until a minimum of patients are included per stratum.

### Study objective

In this study the hypothesis will be tested that
gemcitabine has a radiosensitizing effect in addition to 131I-MIBG therapy which will lead to increased anti-tumour effect in neuroblastoma.

### Study design

Assessment of efficacy will be obtained after 2 cycles (8-9 weeks) and will be recorded as complete response, partial response, stable disease or progressive disease, according to modified International Neuroblastoma Response Criteria (Brodeur et al, 1993).

### Intervention

Patients will be treated with a combination of gemcitabine and 131I-MIBG. Gemcitabine is the IMP in this study.

## Contacts

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## Eligibility criteria

## Inclusion criteria

1. Histological proven neuroblastoma;

2. Measurable primary and/or metastatic disease;

3. Relapsed or progressive neuroblastoma in which standard approaches to treatment have failed;

4. Evidence of sufficient MIBG uptake in bone or soft tissue;

5. 1 year to 18 years of age;

6. Lansky play score >= 70%, or ECOG performance status < 1;

7. Life expectancy >= 6 weeks;

8. Adequate organ function including:

A. Bone marrow: leukocytes > 2.0 x 10 9/L;

B. ANC <1.0 x 10 9/L;

C. Platelets >100 x 10 9/L (in case of bone marrow disease: >75 x 10 9/L);

D. Hepatic: Bilirubin > 1.5x upper limit of normal (ULN); AST, ALT > 5.0x ULN;

E. Renal: Serum creatinine <1.5x ULN for age (1 year to 15 years: <65µmol/L; >15 years: <110µmol/L).

9. Wash out of 3 weeks of prior chemotherapy or radiotherapy (1 week if prior chemotherapy was single agent vincristine), 6 weeks if prior chemotherapy contained nitrosoureas, 6 months since ASCT was given;

10. Able to comply with scheduled follow up and management of toxicity;

11. All patients with reproductive potential must use effective contraception. Female patients with childbearing potential must have negative pregnancy test within 7 days before study treatment;

12. Written informed consent from patients or from parents or legal guardians for minor patients, according to local law and regulations.

### Exclusion criteria

1. Received treatment within the last 21 days with an investigational or conventional anti-cancer drug;

2. Concurrent administration of any other anti-tumour therapy;

3. Serious concomitant disorders that would compromise patient safety;

4. Symptomatic brain metastases;

5. Contra-indication for nuclear isolation;

6. Are pregnant or breastfeeding;

7. 131I-MIBG treatment in prior 3 months;

8. Known hypersensitivity to gemcitabine.

## Study design

### Design

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|---|---|
| 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): | 01-09-2010 |
| Enrollment: | 66 |
| Type: | Anticipated |

# Ethics review

Positive opinion

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| Date: | 21-06-2010 |
| 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 | NL2263 |
| NTR-old | NTR2389 |
| Other | EudraCT : 2007-007974-45 |
| ISRCTN | ISRCTN wordt niet meer aangevraagd. |

# Study results

**Summary results**
N/A