European genetics study of hearing impairment in patients with cancer during childhood treated with cisplatin.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Aural disorders NEC
Study type	Observational non invasive

Summary

ID

NL-OMON41760

Source
ToetsingOnline

Brief title
Genetic variation in ototoxicity after cisplatin treatment in children.

Condition

- Aural disorders NEC
- Miscellaneous and site unspecified neoplasms benign

Synonym
hearing impairment, ototoxicity

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Seventh Framework Programme (FP7)

Intervention

Keyword: Childhood cancer, Cisplatin, Ototoxicity

Outcome measures

Primary outcome

Difference in genetic profile between patients with and without ototoxicity.

Audiograms.

Secondary outcome

Age.

Treatment regimen.

Co-treatment with diuretics and aminoglycosides.

Renal function.

Study description

Background summary

Survival rates after childhood cancer now reach nearly 80% in developed European countries as a result of more effective therapies and better supportive care. However, the treatments that have improved survival are harsh and cause serious side-effects in the long term. Platinum-based chemotherapy is used for a variety of cancers and is questioned by its ototoxic long-term effects, influencing speech and language development, social-emotional development and educational achievement. Hearing loss may affect from 26% to 80% of childhood cancer survivors. Since cisplatin is used in the treatment of several childhood cancer types and the degree of hearing impairment is highly variable in cisplatin-treated patients, it is imperative to identify the patients that are at risk for ototoxicity. The cumulative dose of the anticancer drug, the treatment schedule, the concomitant use of diuretics and aminoglycosides, as well as the patient*s age at diagnosis only partially explain the inter-individual variability in the ototoxic responses. The variation in hearing impairment in similarly treated children, suggests that genetic variation may influence ototoxicity. Currently, the studies that have been performed in children with cancer are based on studies in limited numbers of patients or survivors. Also, previous studies did not include genome-wide

screening, and some studies suffered from selection bias.

Study objective

The aim of this study is to validate known, and identify novel allelic variants which may play a role in the risk of cisplatin-induced ototoxicity in a substantial international cohort of children diagnosed with cancer.

Study design

The study, set up as retrospective and prospective cohort study, is coordinated by the Erasmus Medical Center (EMC), but GWAS will be performed in the EMC and the Universitaetsklinikum Ulm (Germany). In total, we will recruit data from approximately 600 newly diagnosed patients and previously treated patients (survivors), treated with cisplatin-based chemotherapy, without cranial irradiation.

For the detection of gene polymorphisms in this study the participation of individual volunteers includes three pure-tone audiograms as part of routine follow-up visits in the clinic and a single blood sample, simultaneously with a blood sample takenin the context of diagnosis.
In case of refusal of an extra blood sample, participants will be send a saliva kit, including a pre-paid mail-back envelope. Patients can collect the saliva at home or during regular visit at the hospital according to the instructions.
During regular hospital visits a hearing test will be performed three times: before treatment, between the second and the third cycle, and at stop treatment. Audiometry is provided in normal post-closure plan already However, until recently these tests were not carried out at the same time in all children. With this study we want to ensure there will be an improvement in the structure of audiometry.

Once treated patients have given access to their medical recods, audiological data and a single blood sample, data will be collected. In the case of refusal of a single blood sample, participants will be send a saliva kit and will include a pre-paid mail-back envelope. Patients can collect the saliva at home according to the instructions.

Study burden and risks

With relatively simple methods and with minimal load (three times an audiogram during regular hospital visit and a single blood sample, simultaneously with a blood sample taken in the context of patient care), an impression can be obtained from the hearing status and the genetic profile of the patient. The acquired knowledge will help us to answer future questions.

Hearing tests are done as part of the routine follow-up visits in the clinic.

Until recently, the hearing tests were not carried out in every child at the same time during the treatment. With this research, we also want to ensure an improvement in the structure of the hearing tests (before treatment, during treatment and at stop of treatment).

Invasive diagnostic measures or interventions with the patients are not necessary in the context of the study. The study cannot be carried out on adults only since the planned studies are examined in childhood cancer survivors, treated for different types of cancer occurring before age 18. The study will be carried out with these study subjects since we are studying the direct effect and the role of the genetic profile on the development of hearing loss in this specific population.

Contacts

Public
Erasmus Universiteit Rotterdam

Wytemaweg 80
Rotterdam 3000 CB
NL
Scientific
Erasmus Universiteit Rotterdam

Wytemaweg 80
Rotterdam 3000 CB
NL

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

Treated with cisplatin
Diagnosed before the age of 18 years
End-of treatment pure tone audiograms
No radiotherapy administered to head/neck
Normal pre-treatment audiogram

Exclusion criteria

No informed consent
Pre-existing known hearing impairment

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-04-2015
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	19-02-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-07-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-09-2015
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
CCMO	NL50380.078.14