Identification of novel childhood osteosarcoma predisposing genes.

Published: 22-06-2017
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To identify novel childhood osteosarcoma predisposing genes.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skeletal neoplasms malignant and unspecified
Study type	Observational non invasive

Summary

ID

NL-OMON43835

Source
ToetsingOnline

Brief title
Osteosarcoma predisposition

Condition

- Skeletal neoplasms malignant and unspecified

Synonym
bone cancer, osteosarcoma

Research involving
Human

Sponsors and support

Primary sponsor: Genetica
Source(s) of monetary or material Support: stichting Loeka

Intervention

Keyword: Childhood cancer, Genetic predisposition, Osteosarcoma, Whole exome sequencing

Outcome measures

Primary outcome

Understanding the molecular etiology and pathogenesis of CRC in AYAs is expected to yield novel genetic risk factors. that will facilitate clinical decision making, including early tumor detection, in AYAs with CRC and their siblings at risk.

Secondary outcome

Identification of novel genetic risk factors voor CRC will facilitate clinical decision making, including early tumor detection in AYAs with CRC and their siblings at risk.

Study description

Background summary

Osteosarcoma is the sixth leading cause of death in children under the age of 15 years. Several genetic syndromes are known to predispose children to osteosarcoma, e.g. Rothmund Thompson syndrome, Li Fraumeni syndrome, and Retinoblastoma predisposition syndrome. These syndromes are often easily recognizable by a positive family history for cancer or additional features in the patient. The role of cancer predisposition in children with sporadic osteosarcoma, hence without additional features or positive family history, is unknown.

Study objective

To identify novel childhood osteosarcoma predisposing genes.

Study design

We will apply whole exome sequencing on germline DNA of the child with osteosarcoma and both parents. This *trio analysis* enables us to specifically search for de novo and autosomal recessive changes in the DNA of the child, which are likely scenarios for genetic predisposition in sporadic cases. In

addition we will perform whole genome sequencing on tumor DNA. The tumor data will support the identification of osteosarcoma predisposing germline variants, for example by finding genes with second hit mutations in the tumor and by defining recurrent subclasses of osteosarcomas that share somatic mutations or molecular pathways that could be associated with specific deleterious variation in the germline. Candidate genes will be screened in a validation cohort of germline samples from osteosarcoma patients as well as other childhood cancer patients that are available for this study through collection by the AGORA biobank.

Study burden and risks

The risk of this study is considered to be negligible. The only physical burden is a venepuncture. There is a small risk of unsolicited findings when exome or genome sequencing is performed. Patients and/or their caretakers will be thoroughly counselled about these risks and possible psychosocial consequences. Furthermore the protocol that is used for unsolicited findings has already been established in the department of Clinical Genetics and is approved by the Commissie Mensgebonden Onderzoek Regio Arnhem-Nijmegen (ref CD/CMO 0507).

Contacts

Public
Selecteer

Geert Grooteplein 10
Nijmegen 6500HB
NL
Scientific
Selecteer

Geert Grooteplein 10
Nijmegen 6500HB
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

20 individulas who have developed osteosarcoma in childhood (<19 years of age) without a syndrome diagnosis after consultation by a clinical geneticist, and their parents.

Exclusion criteria

- A proven osteosarcoma predisposing condition
- A genetic defect in the family for a cancer unrelated condition, of which the child might be a carrier but about which the child/parents do not want to be informed.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-09-2017
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	22-06-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-07-2017
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

No registrations found.

In other registers

Register	ID
CCMO	NL53280.091.15