PrediCT - Predisposition to Childhood Tumors

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There might be discrepancies in number and type of Cancer Predisposition Syndrome diagnoses between the genotype first and the phenotype first approach.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neoplasm related morbidities
Study type	Observational non invasive

Summary

ID

NL-OMON20548

Source
Nationaal Trial Register

Brief title
PrediCT

Condition

- Neoplasm related morbidities

Health condition

Pediatric cancer/neoplasms

Research involving
Human

Sponsors and support

Primary sponsor: Princes Máxima Center for pediatric oncology
Source(s) of monetary or material Support: KiKa

Intervention

Outcome measures

Primary outcome

Endpoint of this study is determining the performance of a ‘genotype first approach’ in diagnostics of genetic predisposition in children with cancer (unselected for type of tumor), compared to the current ‘phenotype first approach’. We will evaluate the number of identified pediatric cancer predisposition syndromes (CPSs) by the genotype first approach and the phenotype first approach and will focus on discrepancies in diagnoses between these two approaches. Pediatric cancer predisposition syndromes are defined as clinical diagnosis (made by a clinical geneticist) and/or molecular diagnosis (based on targeted tests or WES CPS panel).

Secondary outcome

A. We will evaluate the number of pediatric CPSs diagnosed by the genotype first approach and the phenotype first approach for different groups of tumor types. B. Other secondary study parameters are: - The number of children referred to a clinical geneticists - The number of children who already have a molecular confirmed cancer predisposition syndrome at the time of cancer diagnosis - The total number of pediatric cancer predisposition syndromes - The number of variants of unknown significance (VUSs) detected by WES panel analysis. C. Furthermore we will evaluate the performance of the decision-support questionnaire (MIPOGG tool) on children with cancer who have undergone germline sequencing (WES based CPS panel). The performance of the tool is defined by its capacity to correctly distinguish between those children who do and those who do not have an underlying germline mutation in a cancer susceptibility gene. Based on these endpoints we will develop guidelines for best strategy to detect cancer predisposition syndromes in a routine clinical setting.

Study description

Background summary

Rationale: Recognition of genetic predisposition in children with cancer or neoplasms is of high clinical significance since it might influence therapy choices, surveillance policies and counseling of relatives. Cancer predisposition syndromes (CPSs) can be suspected based on specific hallmarks such as a positive family history or the presence of congenital anomalies. Due to the expanding phenotypic diversity, the upfront ‘phenotype based’ recognition of CPSs is becoming more challenging for clinicians. Furthermore, next-generation sequencing (NGS) studies have revealed mutations in pediatric cancer predisposition genes in patients without any clinical features suggestive for genetic predisposition. Objective: To evaluate the performance of a ‘genotype first approach’ (WES-based panel analysis) in diagnostics of

genetic predisposition in children with cancer or neoplasms, compared to the current ‘phenotype first approach’ (standard of care). In particular we will focus on discrepancies in CPS diagnoses between these two approaches. Study design: Prospective nationwide cohort study. We will use WES-data generated routinely from all children diagnosed with cancer or neoplasms in the Princess Máxima Center. After informed consent, a panel of known pediatric cancer predisposing genes will be analysed in the germline data. Study population: A prospective cohort of children (age < 19 years) who are newly diagnosed with and/or treated for cancer or neoplasms at the Princess Máxima Center in a period of three years. Main study parameters/endpoints: Pediatric cancer predisposition syndromes diagnoses (molecular and/or clinical). We will compare the number of cancer predisposition syndromes diagnosed by the genotype first approach (molecular diagnosis based on WES panel analysis) to the phenotype first approach (clinical diagnosis and/or molecular diagnosis based on targeted tests).

Study objective

There might be discrepancies in number and type of Cancer Predisposition Syndrome diagnoses between the genotype first and the phenotype first approach.

Study design

Not applicable

Intervention

None

Contacts

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Eligibility criteria

Age
Newborns
Newborns
Babies and toddlers (28 days-23 months)
Babies and toddlers (28 days-23 months)
Children (2-11 years)
Children (2-11 years)
Adolescents (12-15 years)
Adolescents (12-15 years)
Adolescents (16-17 years)
Adolescents (16-17 years)

Inclusion criteria

- Children (age < 19 years) newly diagnosed with cancer or neoplasms at the Princess Máxima Center - Written informed consent (by patient when aged 16 years or older, by patient and parent(s) when aged 12-16 years, by parent(s) when younger than 12 years)

Exclusion criteria

- Patients and/or their parents who don't want to know the results of the DNA test (pediatric cancer gene panel analysis)

Study design

Design

Study phase:	N/A
Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-09-2020
Enrollment:	843
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Approved WMO
Application type: Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 52506
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL8456
CCMO	NL70480.041.20
OMON	NL-OMON52506

Study results