DCOG-iTHER: towards Individualized Therapies for Children with Relapsed/Refractory Malignancies using Molecular Profiling

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To analyze the number of patients with (germline/somatic) actionable molecular aberrations in patients with relapsed/refractory pediatric tumors for whom no standard treatment or study protocol is available.

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

Summary

ID

NL-OMON29251

Source
Nationaal Trial Register

Brief title
DCOG-ITHER

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Pediatric Relapsed/Refractory Malignancies

Health condition

relapse refractory, pediatric oncology, molecular profiling, actionable lesions recidief refractair, kinderoncologie, moleculaire profilering, behandelbare laesies

Research involving
Human

Sponsors and support

Primary sponsor: Prinses Máxima Center voor kinderoncologie
Source(s) of monetary or material Support: KiKa, ZonMW

Intervention

- Other intervention

Explanation

Outcome measures

Primary outcome

To define the number of patients with relapsed/refractory pediatric tumors for whom no standard protocol treatment is available, in whom actionable lesions are identified

Secondary outcome

• To determine the number of patients with relapsed/refractory pediatric tumors in the Netherlands each year for whom no standard protocol or treatment is available (per protocol population)

• The percentage of patients who are able to undergo a diagnostic tumor biopsy (as standard of care)

• The percentage of tumor biopsies associated with procedure-related complications

• The percentage of cases in which tumor material was obtained of sufficient quality for molecular profiling

• The percentage of cases in which one or more actionable lesions are identified

• The percentage of cases in which a mutation in a cancer predisposition gene is identified

• The percentage of cases in which the molecular tumor board is able to provide a treatment advice to the treating physician

• The time frame between the date of the biopsy and the date of the treatment advice by the molecular tumor board

• The percentage of patients treated according to the treatment recommendation

• Major side-effects and disease responses observed in the patients treated

• Survival parameters (overall and progression-free survival) in the entire cohort of patients with a follow-up duration of 1 year following enrolment.

Study description

Background summary

Significant progress has been made in the cure of pediatric cancer through treatment optimization (chemotherapy, radiotherapy and surgery) and improvement of supportive care. Despite major advances, 25% of children with cancer ultimately die due to lack of effective treatment. New treatment modalities are urgently needed. The most promising option is the development of targeted therapy in which a genetic aberration in the tumor is targeted by small molecules. This however requires that the tumor biology is deciphered to identify tumor-driving genetic aberrations. Another strategy is to perform compound screening on organoids grown from tumor tissue.

Study objective

To analyze the number of patients with (germline/somatic) actionable molecular aberrations in patients with relapsed/refractory pediatric tumors for whom no standard treatment or study protocol is available.

Study design

This is a non-randomized single-arm observational study aimed at molecular profiling of tumor biopsy samples and germline tissue, taken during a standard of care biopsy procedure to confirm relapsed or refractory malignancy, from patients with relapsed/refractory pediatric tumors.

Intervention

Molecular profiling

Study burden and risks

The main aim of this study is to identify actionable lesions in cancers arising in children to develop personalized medicine. Therefore minors have to be included in the study. There are no risks associated with participation in this study, as the biopsy will be performed as standard of care.

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)
Adults (18-64 years)
Adults (18-64 years)

Inclusion criteria

-relapsed/refractory pediatric cancer, which was established at initial diagnosis by standard diagnostic methods

-no available standard treatment or study protocol

-life-expectancy of at least 10 weeks

-written informed consent according to local law and legislation

-age <30 years

Exclusion criteria

-biopsy considered unsafe

-severe organ toxicity precluding undergoing any of the procedures mentioned in this protocol

-any other condition that may hamper participation according to the treating physician

Study design

Design

Study phase:	N/A
Study type:	Observational non invasive
Intervention model:	Single
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):	18-04-2017
Enrollment:	150
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Approved WMO Date:	09-01-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

ID: 55694
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL5728
NTR-old	NTR5915
CCMO	NL56826.078.16
OMON	NL-OMON55694

Study results

Results posted:	01-02-2024
Actual enrolment:	196

Summary results
"The iTHER program of the Princess Máxima Center demonstrates the establishment of a successful precision medicine program across all ages and tumour types in paediatric oncology that identifies diagnostic, prognostic and targetable alterations as well as reportable germline variants within a clinically relevant timeframe.
Nowadays, all children with newly diagnosed, relapsed or refractory tumours are offered WES

and RNA-seq in our center as standard of care, complemented by DNAmethylation for CNS tumours and sarcomas, to facilitate precision diagnostics and improve cure rates. Standardisation of data analysis and target prioritisation as well as improved access to targeted treatments within combination trials are required to translate findings from precision medicine programs into clinical care and eventually improve survival."

Baseline characteristics
Pediatric relapsed/refractory malignancies

First publication
29-09-2022

URL result
Type
ext
Naam
EJC
URL