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

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To analyse 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 invasive

Summary

ID

NL-OMON55694

Source
ToetsingOnline

Brief title
DCOG-iTHER

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
cancer, relapsed/refractory malignancies

Research involving
Human

Sponsors and support

Primary sponsor: Prinses Máxima Centrum voor Kinderoncologie
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: actionable lesions, Molecular profiling, pediatric oncology, relapse

Outcome measures

Primary outcome

-The number of all included patients in which an actionable lesion could be identified divided by the number of all included patients

Secondary outcome

-The total number of pediatric oncology patients in the Netherlands each year with relapsed/refractory malignant disease for whom no standard protocol or treatment is available (per protocol population)

-The number of patients who are able to undergo a diagnostic tumor biopsy (as standard of care) divided by all included patients (protocol population)

-The number of patients with tumor biopsies associated/procedure-related complications divided by all patients that underwent a tumor biopsy

-The number of patients in which tumor material was obtained of sufficient quality for molecular profiling divided by the total number of patients that underwent a biopsy

-The number of patients in whom actionable lesions were identified divided by the number of patients in who a molecular profile was obtained.

-The number of patients with a germline mutation in a cancer predisposition gene divided by the number of patients in whom germline mutational screening

was successful.

-The number of patients for whom organoid culture is successful divided by the number of patients for whom residual living cells were available for organoid culture.

-The number of patients for whom results from the compound screening are available divided by the number of patients for whom organoid culture was successful.

-The number of patients in which the molecular tumor board is able to provide a treatment advice to the treating physician divided by all patients in whom actionable lesions were identified

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

-The number of patients treated according to the treatment recommendation divided by the total number of patients in which the molecular tumor board provided a treatment advice

-Major side-effects observed in the patients treated will be described.

-Treatment response in solid tumors (complete response, partial response, stable disease or progression) will be assesses using the RECIST criteria.26 In leukemia, complete remission is defined as less than 5% blast cells in the bone marrow.

-Survival parameters overall survival (the percentage of people who are still alive one year after inclusion in the study) and progression-free survival (the time between inclusion in the study until the time that the disease progresses or the patient dies from any cause). Both OS en PFS will be estimated in the

entire cohort of patients using the Kaplan-Meier estimator.

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.

Study objective

To analyse 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.

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. The study consists of molecular profiling of germ line and tumor material with the aim to identify actionable lesions, which will be prioritized by a molecular tumor board. In addition, patient characteristics and clinical follow-up will be collected. If actionable lesions are identified and the patient is treated with a targeted drug (by enrollment in a separate clinical trial, on compassionate use basis, or off-label use of a commercial drug), the patient might benefit from the diagnostics performed in this study. Treatment interventions are not part of this study protocol but data will be captured as part of this registry. In case germ line aberrations are detected and the patient and/or parents have declared they want to be informed, the treating physician will be informed and the

patient/parents will be referred to a clinical geneticist for confirmation of the detected germ line mutation and further counseling.

Contacts

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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

Children and adolescents with pediatric tumors (<30 years of age) can be enrolled into this study when a relapse or a refractory tumor is clinically suspected for whom no standard treatment protocol is available and when informed consent is obtained.

Exclusion criteria

when biopsy is considered unsafe or severe organ toxicity precludes undergoing any of the procedures mentioned in the protocol. Also any other condition that may hamper participation according to the treating physician.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-04-2017
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO

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

Approved WMO

Date:	16-03-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	05-02-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-07-2021
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

ID: 29251
Source: NTR
Title:

In other registers

Register	ID
Other	Nederlands Trial Register 5915
CCMO	NL56826.078.16
OMON	NL-OMON29251