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MyKids: molecular profiling of non-rhabdomyosarcoma soft tissue sarcoma (NRSTS) in children, adolescents and young adults

Submission date 17/06/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 14/07/2022	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 14/07/2022	**Condition category** Cancer	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Soft tissue sarcomas (STS) can arise anywhere in the body. Soft tissues are e.g. muscles, connective tissue, fat tissue or blood vessels. About half of the soft tissue sarcomas in children and young adults are so-called 'rhabdomyosarcomas'. The other half consists of all kinds of different and rare soft tissue sarcomas, the so-called non-rhabdomyosarcoma soft tissue sarcomas (NRSTS).

There is not much known yet about the origin, behaviour and characteristics of this other, very heterogenous, group, the NRSTS, especially in children and young adults where these tumors are extremely rare.

The origin of many types of childhood cancer lies within the genetic composition of the tumor. That is what we call the molecular profile. Therefore, more and more medicines are being developed specifically against certain changes within the genetic material (DNA) or of the macromolecules that are involved in the expression of the genetic information (RNA) of the tumors.

In this study we want to analyze these rare tumors down to the smallest detail in our laboratories. The aim of this study is to make a complete molecular profile of the participants' tumor cells and to make them grow in the laboratory on a petri dish to form an 'organoid'. An organoid is a sort mini-organ cultured from the cells, in this case obtained from the biopsied material.

We hope to learn more about the origin, development and behaviour of these rare tumors and also whether we will be able to detect this tumor with simple blood analysis in the future. It might also become possible to develop targeted drugs against NRSTS in the future, or that already existing drugs could be given to a certain type of tumor based on our findings.

Who can participate?
Patients aged 0 - 25 years, with recently diagnosed NRSTS.

What does the study involve?
Additional blood samples will be collected if the patient consents to participate in WP4, this is optional.

What are the possible benefits and risks of participating?
A possible benefit of participating in this study is that the initial diagnosis is (re)-evaluated by a Diagnostic Advisory Board of experts in the field and that in some individual cases the participant's oncologist might decide to adapt the standard treatment in consequence of the results of the diagnostics performed in the scope of this study.
Furthermore, participation in this study contributes to a better characterization and understanding of NRSTS in children.
The risks of study participation are negligible, as the biopsy will be performed as part of standard of care. Participation in the work packages associated with additional blood sampling is optional. For interpretation of sequencing results, comparison with germline sequencing is needed, for which an extra tube of blood is needed, to be collected in combination with regular blood withdrawals. In most countries this is already included in the standard of care.
Additional material collected for study purposes are the blood samples for the detection of circulating tumor DNA (liquid biopsies; WP4). These blood withdrawals will be combined with standard of care blood withdrawals as much as possible.

Where is the study run from?
Princess Máxima Center (Netherlands)

When is the study starting and how long is it expected to run for?
January 2022 to September 2030

Who is funding the study?
KiKa - Stichting Kinderen Kankervrij (Netherlands)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Protocol serial number
NL81255.041.22

Study information

Scientific Title
MyKids: molecular identification and characterization of non-rhabdomyosarcoma soft tissue sarcoma in kids, adolescents and young adults: an EpSSG NRSTS study

Acronym
MyKids

Study objectives
The overall aim is to better understand the potential for molecular diagnosis of pediatric NRSTS with a view to optimize treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Primary study design
Observational

Study design
International multicenter prospective study

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Non-Rhabdomyosarcoma Soft Tissue Sarcoma (NRSTS)

Interventions
At primary diagnosis, part of the biopsy material obtained for standard care will be used for the study (see primary outcome measures) and an additional tube of blood will be drawn for the study.
Participation in work packages 1, 3, 4 and 5 is optional. If the participant has given consent to participate in work package 4 (liquid biopsies), additional blood sampling will take place at diagnosis, during and after the standard treatment and will be combined with the standard care venipunctures as much as possible. The exact amount of venipunctures depends on the treatment duration. The follow-up period is at least 4 years.

Intervention Type
Genetic

Primary outcome(s)

WP1
1. Gene expression changes, measured as expression score, by bulk mRNA sequencing at primary diagnosis.
2. Genetic alterations (e.g. copy number variations, SNVs, fusions, translocations), measured by Whole Exome Sequencing (WES) at primary diagnosis.
3. Epigenetic alterations (methylation patterns), measured by DNA Methylation profiling (DNAmeth) at primary diagnosis.
4. Comparison of diagnoses (diagnostic terms) established by before-mentioned molecular techinques to diagnoses established by conventional histology/pathology at primary diagnosis.

WP2
5. Molecular diagnosis on FFPE material (gene expression changes, measured as expression score) by mRNA sequencing at primary diagnosis.
6. Genomic index, measured as comparative gene expression signature, by Comparative Genome Hybridization (aGCH) at primary diagnosis.
7. Fédération Nationale des Centers de Lutte Contre le Cancer (FNCLCC) grading, determined by pathological grading at primary diagnosis.
8. CINSARC signature (a 67-gene signature related to chromosome integrity and genome complexity) - detection by comparing prognostic value compared to CINSARC and pathological grading at primary diagnosis.

WP3
9. Percentage of successful tumoroid models cultured (tumoroid culture successful or not) by basic mathematic analysis (percentages) at primary diagnosis.
10. Single cell mRNA sequencing of tumoroids (comparison of gene expression profiles between single cells and clustering into sub-populations) at primary diagnosis.

WP4
11. Identification of possible patient specific, individually expressed ctDNA markers, by data analysis of molecular diagnostics on FFPE material and peripheral blood samples (DNA methylation profiling, WES, copy number profiling, assessment of patient specific breaking points) at primary diagnosis.
12. ctDNA marker measurement (e.g. DNA methylation profiling, WES, copy number profiling, assessment of patient specific breaking points) in peripheral blood at primary diagnosis, during treatment at regular evaluation moments (frequency depends on treatment), during follow-up (1x/year during 2 years) and at relapse or progressive disease.

WP5
13. Gene expression changes, measured as expression score, by bulk mRNA sequencing at tumor-resection surgery (post-treatment)
14. Genetic alterations (e.g. copy number variations, SNVs, fusions, translocations), measured by Whole Exome Sequencing (WES) at tumor-resection surgery (post-treatment).
15. Epigenetic alterations (methylation patterns), measured by DNA Methylation profiling (DNAmeth) at tumor-resection surgery (post-treatment).

Key secondary outcome(s)
There are no secondary outcome measures

Completion date
01/09/2030

Eligibility

Key inclusion criteria
1. Patients within 2 months after new diagnosis of NRSTS
2. Age 0 - 25 years
3. Written informed consent by parents/legal representatives and patients 12 year and older
4. Minimal requirements for study participation: diagnostic FFPE material for WP2 or fresh frozen sample for WP1

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
0 Years

Upper age limit
25 Years

Sex
All

Key exclusion criteria
1. Relapsed NRSTS, not included at diagnosis
2. No written informed consent

Date of first enrolment
01/09/2022

Date of final enrolment
01/09/2026

Locations

Countries of recruitment
United Kingdom

Argentina

Australia

Belgium

Czech Republic

Denmark

France

Greece

Israel

Italy

Netherlands

Norway

Portugal

Slovakia

Slovenia

Spain

Switzerland

Study participating centre
Princess Máxima Center for pediatric oncology
Heidelberglaan 25
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Sponsor information

Organisation
Princess Máxima Center

ROR
https://ror.org/02aj7yc53

Funder(s)

Funder type
Charity

Funder Name
Stichting Kinderen Kankervrij

Alternative Name(s)
Children Cancer Free Foundation, Foundation KiKa, Kika8118, Kiki_KinderenKankervrij, Stichting Kinderen Kankervrij (KiKa), KiKa

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Netherlands

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date