Medizinische Hochschule Hannover

KiTZ Hopp-Kindertumorzentrum Heidelberg
Deutsches Krebsforschungszentrum
Universitätsklinikum Heidelberg
Universität Heidelberg

Forschung Information Therapie

Krebsprädispositionssyndrom-Register 01

Registerleitung:
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Prof. Dr. med. Stefan Pfister

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Information for children 7-11 years of age

Cancer-Predisposition-Syndrome-Registry 01

Dear_____,

You have surely just noticed that you and your parents are being asked to participate in a registry. This sheet should explain, what this means. You can read everything on your own, think about it and discuss it with your parents and your treating physicians whether you would like to participate.

Your physicians have discovered that you have a rare disease. There are only a few children who have the same disease. So now, physicians in Germany and all over the world are working together to better understand this disease and to help you and the other children, who have the same illness as you. They want to collect as much and precise information as possible about children with this rare disease to improve how to find it and how to make the children healthy again. The physicians also want to store and examine your blood and other body cells. But you will not be pricked especially for this.
If you want to participate, your physicians would give us documents about you and your medical story so that we can examine you illness in detail.

We would be happy if you would like to participate and help other children as well. But if you don't want to, that is no problem either. Please ask your doctors if there is something you don't understand. They will gladly help you.

Thank you very much.
Your team of physicians

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Information for parents/guardians

Cancer-Predisposition-Syndrome-Registry-01

Dear Parents/Guardians,
The physician of your child has informed you that your child has been diagnosed with a cancer predisposition syndrome. One main feature of this genetic condition is an increased cancer risk.
The medical care for individuals with cancer predisposition syndromes has not been standardized in the past. For specific cancer predisposition syndromes, participation in surveillance programs may be useful to detect and treat cancer(s) at an early stage.

Our registry has been established in order to pursue the following aims:

- To assemble a database with medical and genetic information from a large group of individuals with cancer predisposition syndromes. By doing so, we learn the natural history of cancer predisposition syndromes. The resulting knowledge will be used to create recommendations for patients and health care professionals.
- To offer advice to your child's physicians regarding the evaluation and interpretation of important findings related to your child's health. Due to the fact that we receive, evaluate and interpret a large number of such findings, we hope that our analysis may improve the quality of your child's medical care.
- To collect blood samples and (if applicable) bone marrow and tumor specimens from patients with a cancer predisposition syndrome for research purposes. Our research aims to better understand the basic genetics of cancer predisposition syndromes. For example, not all cancer predisposition syndrome causing genes are known. In addition, many of the genetic factors that negatively or positively influence the clinical course of patients with a cancer predisposition syndrome remain unidentified. Therefore, we aim at uncovering these modifying factors. Finally, by genetically analyzing tumor specimens from individuals with a cancer predisposition syndrome, we endeavor to discover the tumor-specific molecular mechanisms leading to cancer.

Brief Overview

Current state of knowledge: More than 50 cancer predisposition syndromes have been described. For many of these conditions, the precise cancer risks are unknown. For several cancer predisposing conditions, cancer surveillance strategies are recommended; however, little is known about the effectiveness of these recommendations. In addition, the genetic principales of cancer predisposition as well as the molecular mechanisms in cancer cells in patients with these conditions are poorly understood.

Study design: Our registry represents a natural history study. We collect medical information, radiological images and findings, genetic testing results, biospecimen such as blood and if available, bone marrow and tumor specimens from individuals with a cancer predisposition syndrome, in order to learn more about cancer predisposition syndromes and their associated cancers.

Procedures and processes: Only medical procedures that represent current standard of care for your child's condition are conducted. At the time that blood draws are normally completed for your child's medical care, additional blood samples will be taken and stored for research purposes. Medical information that is generated through the standard care of your child's condition, as well as genetic testing results and blood/ tissue specimen, will be transferred to the registry. Since this is a long-term investigation that addresses the course of a condition over several years, the study has no defined duration. Therefore, results from follow-up investigations will be collected by the registry.
The registry collects information from multiple individuals with cancer predisposition syndromes, which results in generating knowledge related to the long-term course of different cancer predisposition syndromes.

The Risks and Benefits of Participation

Expected individual benefit:
Donating your child's biospecimen and medical data will not necessarily lead to a direct benefit to your child. Our analysis serves primarily as scientific research and is not intended as actionable conclusions for your child's health. Nevertheless, the research may lead to findings that may be of importance to your child's health. In the situation, when an analysis reveals evidence of a severe previously unknown condition, that can potentially be treated or prevented, we may want to contact you in order to give you this information (see below).

In case you do not wish to receive this type of feedback, please check the box containing "no" on the informed consent. At any time, you can change your decision for or against this feedback option by letting us know. However, please note that you may be obligated to disclose health related information that you receive through our registry, to other parties such as health- or life insurance companies. This may be a disadvantage for your child.

The statement above is also relevant to genetic analyses and the discovery of genetic conditions. Therefore, this information may be relevant for family members and family planning.

In the long-term, biospecimen and data collected through our registry is meant eventually to improve the care of patients with cancer predisposition syndromes (possibly including participants of the registry). For example, we would like to explore the role of regular evidence-based surveillance strategies.

In addition, we offer your treatment team to assess important findings. By receiving and evaluating a lot of these examinations, we have a comparatively broad experience with the disease. Therefore, we expect a high quality of our assessment and a benefit for your care.

General Benefit of the Registry:
Medical studies of this kind aim at better understanding processes associated with disease development and improvement in diagnosis and care. Other patients with cancer predisposition syndromes not participating in this research may benefit from our findings because our research aims at improving the care of all affected patients. Through the collection of biospecimen from individuals with a cancer predisposition syndrome, cancer research in general is driven forward. There may be benefits for patients with cancer even in the absence of a cancer predisposition syndrome. We know that molecular mechanism playing a role in cancer predisposition syndromes may also be relevant for cancer patients in general. In theory, it is possible that our research contributes to an improved therapy and prognosis of cancer patients.

Risks and Disadvantages of participation:
Blood draws are usually performed throughout your child's medical care. On these occasions, we would like to collect an extra 5-10 ml (one to two teaspoons) of blood for our biobank. This extra blood does not lead to extra risk for your child. Since our study is a natural history study, there are no additional physical risks.

A tumor specimen is collected for research purposes only when a biopsy or tumor resection is performed as part of standard medical care. The size of the collected tumor specimen cannot be predicted as it depends on the size of the removed tumor sample. It is assured that research samples will be collected only if there is sufficient tumor material for diagnostic and therapeutic decisions. Therefore, the collection of tumor specimen for our registry does not impose additional risks.

Every collection, storage and transfer of data is associated with the risk of breaching the confidentiality (e.g. risk of identifying your person/information), which may be especially relevant for genetic information. It is impossible to entirely exclude this type of risk. This risk increases with the amount of connected data, especially if you are publishing genetic information in the internet on your own.

Purpose of collecting biospecimen:
Collected blood and tissue samples will be stored. Research will be conducted on the mechanisms of cancer development utilizing these materials. Your samples might be used to produce long-living cell culture, to investigate the behavior of cells for example when exposed to specific drugs. The sample are reserved for research related to the underlying condition. For example, we would like to determine why certain individuals with a cancer predisposition have higher cancer risks than others with the same condition. Also, we would like to elucidate molecular mechanisms of cancer development in cells. Genetic studies may be conducted that may involve studies of whole genome. Samples and data will be available for research purposes for an undetermined period of time.

Protection of your child's biospecimen and data:
Biospecimen will be stored in the Biobank of Hannover Medical School of indefinite duration. Clinical data will be stored on a secured sever of XClinical (biomedical software engineers of MARVIN, the main data management system of the German Society of Pediatric Oncology and Hematology). Only your birth quarter

and year and your gender are electronically recorded as "personal data". We explicitly do not record any names in the database. Your identifying data will only be shared with principle investigator of the repective cancer treatment study, the relevant state cancer registry and the German Childhood Cancer Registry (DKKR) in Mainz. Personal information will not be shared with researchers or other unauthorized third parties, such as insurance companies or employers. All identifying information (name, date of birth, address, etc.) will be replaced by a code for research purposes. Only after this process, biospecimen and data will be made available for research.

Only coded biospecimen and data are used for research conducted by universities, research institutes or companies. It is possible that our registry data will be connected to your child's data in other databases, in accordance with the law and appropriate ethic committee approvals. For example, if your child has a tumor for which your child is receiving treatment on a clinical trial, information entered for this trail may be coupled our database and vice versa. Authorization to use biospecimen and data in a research study is limited to a specific researcher and project. The researcher is prohibited from using or passing on the biospecimen and data for additional purposes without permission. Remaining material is returned to the Hannover Medical School biobank or is destroyed.

Prior to using the biospecimen and data for a research project, a researcher must obtain an institutional ethics board approval. Institutional ethics board approval ensures that appropriate steps are taken to protect the rights and welfare of subjects of a research study.

Publications are written in an anonymized fashion to prohibit identification of individual participants. This implies the situation, if data is entered into scientific online databases. A publication of your child's entire genetic information (genome) is impossible without your explicit written permission.

In order to consult with your child's physician regarding your child's medical care, our registry keeps a locked file with identifying information (e.g. name, date of birth, address). All data directly identifying your person (name, date of birth, address, etc.) will be replaced by an identification code (pseudonymized) immediately after obtaining the biomaterials. Only in this form are the biomaterials and data made available for research purposes.**If you live in Germany, identifying information may be exchanged with the study group that is in charge of your cancer treatment plan, the states cancer registry and the German Childhood Cancer Registry in Mainz**.

Deutsches Kinderkrebsregister
Abteilung Epidemiologie von Krebs im Kindesalter (EpiKiK)
Institut für Medizinische Biometrie, Epidemiologie und Informatik(IMBEI)
UNIVERSITÄTSMEDIZIN der Johannes Gutenberg-Universität Mainz
Leitung: Dr. Friederike Erdmann

Financial benefits to you or the biobank:
You will not be paid for allowing us to collect and store your child's biospecimen and data. You will not receive financial or other compensation, should findings resulting from the research on your child's biospecimen become commercially valuable. By providing your child's biospecimen in the Biobank of Hannover Medical School they become the property of the CPS-R01 registry of the German Society of Pediatric Oncology and

Hematology. Specimen and data will only be used for research not be sold. However, the biobank can ask researchers for an expense allowance for providing specimen to collaborating researchers.

Other Questions and Concerns

Is it possible that you will be contacted regarding the registry?
On a regular basis, results from your child's medical visits are being forwarded to the registry team. In case of missing data, it could be useful that you are contacted at a later time point in order to request additional information or specimen. Also, this contact could occur to request your permission for connecting your child's data with other databases or in order to give feedback to you or your physician on findings that may be relevant to your child's health. You will not be contacted through the registry team directly but through your child's physician or the health care institution that cares for your child.

In case you do not wish to be contacted, please check the box containing "no" on the informed consent.

What is your right of withdrawal from the registry?
Any time and without justification and disadvantages you may withdraw your consent that allows us to use your child's biospecimen and data. In case you withdraw your consent, you may decide whether your child's specimen should be destroyed or be anonymized. In the latter situation, we delete the identification code that allows us to connect a specimen to your child. One has to keep in mind that such an anonymization process cannot entirely exclude the small chance that a specimen can be tracked back to your child.
You can also decide whether your already collected data should be deleted or may be further used in anonymized form. Data can only be deleted under the conditions of Art. 17 DSGVO.

As soon as the purchase of the biomaterials and other data relating to your child's person has been deleted (anonymization), destruction is no longer possible. In addition, data from analyses already carried out can no longer be removed.

In case you would like to withdraw your consent, please contact:

Christian P. Kratz, MD, Director
Pediatric Hematology and Oncology
Hannover Medical School
Carl-Neuberg-Str. 1
30625 Hannover
Germany
Phone: +49 (0)511 532 6711
Fax: +49 (0)511 532 9120
Email: kratz.christian@mh-hannover.de

Is your participation voluntary?
Your participation in this registry is voluntary. In case you prefer not to participate, your child will experience no disadvantage.

Where can I get additional information?

Should you have additional questions, please contact your physician prior to giving your consent. You can also contact Prof. Kratz or Prof. Pfister. Information regarding findings can be found on www.krebs-praedisposition.de.

We are happy to address your questions.

Sincerely

Christian Kratz, MD Stefan Pfister, MD

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Im Neuenheimer Feld 580, 69120 Heidelberg

Informed consent for parents/guardians

Enrollment in Cancer-Predisposition–Syndrome-R01

_____ _____
Patient (Last Name, First Name) Date of Birth (dd/mm/yy)

_____
Treating Hospital

I have read the information sheet and had the opportunity to ask questions. My questions were answered comprehensively and comprehensibly. I know that my child's participation is voluntary and that I can retract my consent any time without justification and without disadvantages. I had enough time to consider my decision to participate and make my own decision.

I give my informed consent that my child's biospecimen as well as medical information as described in the information sheet are sent to the CPS-R01 to be used for medical research purposes.

I give my consent that the scientific projects, for which the biospecimen and medical information will be used, serve scientific and medical purposes.

I transfer ownership of the biospecimen to the CPS-R01 of the German Society of Pediatric Oncology and Hematology.

I approve that I may be contacted at a later point in time for the following reasons, please check the boxes with “yes” or “no”:

- For the collection of additional medical information/biospecimen □ yes □ no
- If further consent is necessary for the use of your child’s medical information □ yes □ no
- If our research identifies findings that may be relevant to your child’s health □ yes □ no

This contact should occur through the institution that collected my child’s biospecimen and data **or** by the following physician (please give this information to the physician if the latter is preferred):

Physician name and address: _____

Data Protection Statement

I approve that the registry team conducts the following actions (also described in the information sheet):

- enters only initials, as well as quarter and year of birth in the registry data base

- Collects and stores identifying materials and information related to my child’s health

- Extracts additional health related data containing identifying information from my child’s medical records

- After collection, biospecimen and data will pseudonymized to be used for medical research purposes

- Exchanges basic data on diagnosis and follow-up with the therapy reatment study of the corresponding cancer, with the state cancer registry and with the German Childhood Cancer Registry

- Coded non-identifying information can be used for scientific publications and online databases

My child’s biospecimen and data may be used for medical research purposes for an unlimited time period.

In a non-identifiable manner, biospecimen and data may be transferred to universities, research institutes/companies for the purpose of medical research. This may include international research projects with lower data protection standards.

I was informed that I may withdraw my consent to participate in the registry any time without justification. In case of withdrawal, I may request that any remaining biospecimen and data be destroyed, deleted or anonymized.

Please note: If an analysis has been completed, your data cannot be removed.

I have the right to be informed about the stored personal data concerning my child (Art. 15 DS-GVO). If I discover that incorrect personal data of my child is being processed, I can demand correction (Art. 16 DS-GVO).

I have the right to demand the deletion of personal data if certain reasons for deletion exist. This is the case, for example, if the personal data are no longer necessary for the purpose for which they were originally collected or processed, or if I revoke my consent and there is no other legal basis for the processing (Art. 17 DS-GVO). Furthermore, I have the right to limit the processing of my child's personal data (Art. 18 DS-GVO), to data transferability (Art. 20 DS-GVO) and a general right of objection (Art. 21 DS-GVO).

Data controller: Christian Kratz, MD
Pediatric Hematology and Oncology, OE 6780
Carl-Neuberg-Straße 1
30625 Hannover
Germany

If I have any questions or if I have the opinion that the processing of my child's personal data is not lawful, I have the option of contacting the MHH data protection officer:

Datenschutzbeauftragte der MHH
OE 0007
Carl-Neuberg-Straße 1
30625 Hannover
Germany

I have the right to complain at the supervisory authority if I believe that the processing of my child's personal data is not lawful.
The address of the supervisory authority responsible for the MHH is:

Die Landesbeauftragte für den Datenschutz Niedersachsen
Prinzenstraße 5
30159 Hannover
Germany

I am aware that the data protection regulations set out in the information letter also applies.

I have received a copy of the information sheet and the signed informed consent. The original is kept in the patient's medical record.

In addition, I was orally informed about the study.

CONFIRMATION OF THE PARENT/GUARDIAN

_____

Patient name (in block capitals)

_____ _____

Place, date Signature parent/guardian

CONFIRMATION FROM THE ATTENDING PHYSICIAN

I have discussed the registry CPS-R01 and the accompanying research including the patient information and the declaration of consent with the custodians. All questions were answered comprehensively. I have explained to the guardians that participation is voluntary. I have obtained the consent of the legal guardian.

_____

Name of physician (in block capitals)

_____ _____

Place, date Signature of attending physician