PTT2.0

INFORMATION FOR PATIENTS
18 YEARS AND OLDER

„Pediatric Targeted Therapy 2.0“ – personalized pediatric oncology: targeted therapy and clinical feasibility.

__________________________  ______________________  ______________________
Name                  First name                   DOB

Dear Mr., dear Mrs. …………………………………………,

thank you for reading the information on PTT2.0. Please take the time to decide, whether you should participate in this study. Discuss your decision also with your family and friends, if this is helpful to you. Please do not hesitate to ask us all your questions, which can help you make your decision.

1. What is PTT2.0?
The purpose of the PTT2.0 study is the collection of research data to improve our knowledge on genetic alterations in relapsed and progressive childhood tumors. The data collected here will enable the development of new treatment strategies for patients, individualized cancer therapy and risk stratification in the future. This study has been reviewed and approved by the ethics committee of the Medical Faculty of the University of Heidelberg.

2. What are the goals of the PTT2.0 study?

It is widely accepted that cancer is a disease resulting from genetic and epigenetic changes (i.e. changes in factors controlling genetic information) in the cells that make up the body. In this study, researchers are trying to understand these specific genetic and epigenetic changes in tumors, and are looking for changes that can be exploited for targeted therapies (which selectively interfere with the specific changes in a tumor, as opposed to chemotherapy).
We suppose that in the near future, the tumor and the blood of all cancer patients will be analyzed in such a manner, in order to treat each patient as individually as possible.

In order to be prepared for this new era, and also to benefit today from these technical possibilities at least in part, we introduce these analyses in the PTT2.0 study. Our goal is to achieve a turnaround time of 4 weeks for the analysis of the genetic information and clinical evaluation of the changes discovered. At the same time we want to collect data on possible therapies and how to implement them.

The decision about if and which kind of therapy is given to you based on the genetic analysis, lies solely with your treating physician. The targets identified by the genetic analysis can be used by your treating physician for his decision.

We want to document your clinical course, irrespective of which treatment you receive, in order to compare the application of targeted therapies to standard chemotherapies, as well as to compare the actionability of the different targets found. By collecting this data, we hope to:

a) learn more about the genetic structure of pediatric tumors,
b) identify common and actionable targets
c) and identify most promising therapeutic strategies.

3. Why were you selected?
You were selected because you were diagnosed with cancer refractory to standard of care treatment. Therefore, the genetic information of your tumor obtained via PTT2.0 might be used to select novel therapeutic approaches. The consent to participate is voluntary and can be withdrawn at any time without reason, which will bear no disadvantages for you.

4. What does the participation include?
Your participation in the PTT2.0 study requires the consent to participate in the following three points:

A. Use of archived tissue samples: Your consent to participate will allow us to analyze the tissue obtained during a planned surgical or other procedure performed during the diagnostic workup upon primary diagnosis or recurrence of your tumor (e.g. stereotactic biopsy). This means that no tissue will be obtained specifically for the PTT2.0 study. Only residual material that is not being used for diagnostics will be used. With this consent you will also allow us to analyze previously gained samples (such as the primary tumor, first, second recurrence etc.), should they exist.
B. Analysis of a blood sample: Your consent to participate will allow us to analyze your blood, approx. 5ml (corresponding to approx. 1 tea spoon) for this study. The blood will be gained during routine blood sampling. The genetic information (DNA) from the blood will be extracted. The DNA will be used for targeted sequencing, which is a process that will allow us to identify many changes unique to you, which distinguish your DNA from the DNA of other people. We need this information in order to identify changes in the tumor, which are not detectable in normal tissue.

C. Clinical Data: Your consent to participate will allow us to collect relevant information on your health and disease in this study. This information can be collected e.g. from hospital files, and can be send from your treating hospital directly to us.

5. How will the data and samples be stored and protected?
All your collected tissue and blood samples will be analyzed during routine diagnostics. All doctors and scientists working with these samples are bound to data protection. All samples will be sent back to the submitting institution after completion of diagnostics and validation. Your data as well as all results from the analyses are stored in a protected database at the German Cancer Research Center (DKFZ), and stored for at least 10 years after the end of this study.

6. Who is allowed to use the data of your child?
One of the goals of the PTT2.0 study is to share anonymized data with other researchers (national and international academic researchers), in order to facilitate and accelerate the investigation of the causes and potential therapies of cancer. However, the PTT2.0 study group also respects the individuals providing their samples for this project, and will ensure their privacy. To achieve this, all personal identifiers, such as your name or address will be removed, and replaced by a unique identifier (pseudonymization). Pseudonymization means that a code consisting of numbers and/or letters will be used, possibly in combination with the year of birth (but not the complete date of birth). Only the PTT2.0 study group will be able to connect this code with information that can be used to identify you. The coded data will be stored in two separate databases, public databases and databases with controlled access.

• Public databases: Information from this databases is publically available, but can not be used to identify you specifically. Only data on e.g. kind of tumor, age group, tumor specific mutations can be found here.
• **Databases with controlled access:** The data will only be accessible to researchers, and only be used for the study of causes of and therapeutic options for cancer.

All results from research based on data from the PTT2.0 study can be used for teaching, research, and publication including presentation at e.g. research meetings. In all cases of publication your identity remains confidential.

7. **What is the benefit of your participation?**

The biggest health-related benefit of the PTT2.0 study will only be accessible in a few years, and as such only the next patient generation will fully benefit from the results. However, should we detect changes in your genetic information, which could inform your current treatment, this information can be used by your treating physician.

8. **What are the risks for you?**

Physical risks: since we only use tissues and blood samples, that are collected during routine procedures that are conducted for diagnostic purposes independent of this study, there are practically no risks for you. The storage of the tissue and blood samples poses only a minimal risk, since a high level of security measures are taken to protect stored specimens from unauthorized access at the German Cancer Research Center (DKFZ), the University Hospital Heidelberg, and the National Center of Tumor diseases (NCT).

Protection of privacy: There is a minimal risk, that genetic information generated in the PTT2.0 study can be connected to genetic or medical information from other databases. It is theoretically possible, however very unlikely, that security measures used to protect the data stored in the data bases, are broken. Of course no employer, insurance agency, or non-authorized family members will get access to this data.

9. **What happens if something is detected in my tumor or in my normal tissue?**

A. **Information that can be used for diagnostics and therapy**

As described under (7), your treating physician has access to the results of the PTT2.0 study. Therefore you can gain access to the data through your treating physician, if the analyses reveal a clear clinical benefit concerning the treatment of your tumor disease. The molecular genetic data may only be used for therapeutic purposes. We can only evaluate the clinical benefit once at the time of analysis, not over and over. In this respect, we cannot guarantee an access to the data, if the changing scientific consensus indicates a clinical benefit.
B. Signs of heritable disease:
If the clinically usable information possibly concerns other family members (e.g. heritable susceptibility for (other) cancer diseases, such as breast or colon cancer), and you have consented to be informed about such a result, these results will be communicated to you in a human genetics counselling session. This only applies if you have explicitly consented to this procedure.
In the unlikely event that potential risk factors for other diseases, not related to the tumor disease, are found in the DNA, these will not be communicated to you.
The analysis of the submitted blood samples may lead to the identification of markers of heritable tumor diseases. These are not limited to tumor cells and represent changes that are present in all cells of the body. The diagnosis of a heritable tumor disease with your child may have an impact on other family members and for example indicate early cancer screenings for relatives.
Heritable elements of tumor diseases may be associated with a higher risk of development of different tumors or, in some cases, may cause other diseases. Such findings will be communicated and explained by specialists during a human genetics counseling session. Well known examples of heritable alterations occur for example in the genes TP53 (cause for the Li Fraumeni Syndrome), and BRCA1/2 (cause of heritable breast and ovarian cancer) or NF1 (cause of neurofibromatosis 1). Heritable factors have been explained during the informed consent discussion.
In the case markers indicating a heritable tumor disease are identified, DNA from tumor and blood sample will be sent to the Department of Human Genetics, where this diagnosis will be validated in a qualified diagnostics laboratory in accordance with the German Genetic Diagnostic Act (Gendiagnostikgesetz). The Department of Human Genetics will inform the treating physicians about any validated findings and will offer genetic counseling at the institute's clinics in Heidelberg or alternatively at a location close to the patients home address.
If you have questions concerning the identification of hereditary gene alterations please contact the Department of Human Genetics (Director: Prof. C.R. Bartram, Tel.: +49-6221-56-5152; E-Mail: Cr.Bartram@med.uni-heidelberg.de).

10. Will you be paid for participation?
Participation is on a strictly voluntary basis, no payments are made.

11. How can you withdraw your consent to participate in the study?
You can withdraw your consent to participate in the PTT2.0 study at any time without need for giving a reason. Please inform your treating physician. If you withdraw your consent, your remaining samples will be destroyed. Data that have already been generated as well as collected clinical data cannot be withdrawn, however no new information will be added to the PTT2.0 database. Your identifiers, such as name, address, complete date of birth, will be deleted. If the data have already been added to a different database, a connection of the data to you will not be possible anymore.

12. What can you do in case of second thoughts?
If you first decide to participate in this study, and have second thoughts in the future, you can always contact us by phone (+49 6221-423387 (Dr. med. Jonas Ecker) or +49 6221-5637429 (PD Dr. med. Till Milde), or by email (j.ecker@dkfz.de or t.milde@dkfz.de).

Contact/Investigator
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INFORMED CONSENT FOR PATIENTS 18 YEARS AND OLDER

„Pediatric Targeted Therapy 2.0“ – personalized pediatric oncology: targeted therapy and clinical feasibility.

Dr. ______________________________ explained the PTT2.0 program to me. The consent for participation in PTT2.0 program is fully voluntary. I have received written information about the program and have read it. I was allowed to ask questions about the program, which were all answered sufficiently.

With my signature I agree that my tumor material and blood is used for research purpose. Archived tumor material gained at a previous time point may be analyzed as well.

I have been informed and consent that my data are used and analyzed for this study. The data may be passed to other researchers in pseudonymized form for research purposes. Pseudonymization means that a code consisting of numbers and/or letters will be used, possibly in combination with the year of birth (but not the complete date of birth). No third party will have access to personal records. In case of publication, my identity will remain anonymous. All data as well as the results of analysis of my child were stored for at least 10 years after closing the registry.

I want to be informed about (at the time of analysis) clinically usable changes found in the tumor tissue.

I want to be informed, if my tumor sample and my blood exhibit evidence for the presence of a hereditary tumor-related syndrome. For this purpose DNA extracted from tumor tissue and blood sample will be forwarded to the Institute of Human Genetics, University Hospital Heidelberg, for validation of the findings by a qualified diagnostics laboratory and according to the German Genetic Diagnostic Act (Gen-Diagnostikgesetz, G-DG).

☐ Yes, I want to be informed.
☐ No, I don't want to be informed.

I agree to my participation in the study. I will receive a copy of this informed consent with my signature.
Personal data of participant

Name and first name________________________________________________________
DOB_____________________________________________________________________

Date_____________ Signature (mother)_____________________________________

Confirmation of the treating physician

I have explained the PTT2.0 study including the participation requirements to the participant. All questions have been fully answered. I have explained to the participant that the participation is fully voluntary.

Name of the treating physician ____________________________________________

Date_____________ Signature_____________________________________________

Approval

The PTT2.0 Study has been submitted to the ethics committee of the University of Heidelberg and approved on XX.XX.XXXX

INFORMATION ON THE TRANSLATOR (IF APPLICABLE)

I was present in the informed consent discussion between Dr. ______________ and the participant. I have translated the patient information to the participant and have elucidated all information contained.

Name of the translator____________________________________________________

Date_____________ Signature_____________________________________________