

## **Parental information<sup>1</sup> and consent form for participation in the registry study**

### **Functional testing of variants of unclear significance in the *ALPL* gene as a cause of hypophosphatasia.**

Dear Parents!

We invite your child to participate in the above-mentioned registry study. You will be informed about this in a detailed medical consultation.

**Your child's participation in this registry study is voluntary. You can withdraw from the study at any time without giving reasons. Refusal to participate or early withdrawal from this study will not adversely affect your child's medical care.**

Clinical trials are necessary to obtain reliable new medical research results. However, an indispensable prerequisite for conducting a clinical trial is that you give your written consent for your child to participate in this study. Please read the following text carefully as a supplement to the informational interview with your physician and do not hesitate to ask questions.

Please sign the consent form only

- if you fully understand the nature and procedure of the clinical study,
- if you are willing to consent to your child's participation, and
- you are aware of your rights as a parent of a participant in this clinical trial.

A favorable opinion on this clinical study, as well as on the patient information and consent form, has been issued by the responsible ethics committee.

#### **1. What is the purpose of the clinical trial?**

The rare, inherited disease hypophosphatasia (HPP) is caused by disease-causing mutations in the *ALPL* gene. Your child has been found to have a genetic variant of unclear significance (VUS) in the *ALPL* gene, meaning it is not clear whether or not this gene variant is disease-causing. This study investigates such VUS to find out whether they are disease-causing or not. The presence of VUS is one of the reasons why HPP, like many other genetic diseases, is often diagnosed years late. Early diagnosis by genetic testing allows early referral to, and intervention by, the, specialist. The results of this study will contribute to improved diagnosis and ultimately improved clinical management of the disease, and reduce the burden on the health care system.

#### **2. How does the clinical study proceed?**

The study center is the research laboratory of the Department of Pediatrics and Adolescent Medicine at the Johannes Kepler University (JKU) Linz, which performs the testing of genetic variants that will make it possible to determine whether a VUS is disease-causing or not. The genetic code of your child's VUS will also be sent to this laboratory, along with pseudonymized

---

<sup>1</sup> For the sake of better readability, the simultaneous use of feminine and masculine personal terms has been partially dispensed with in the remainder of the text. Where applicable, this always refers to both genders.

information about your child's clinical picture. This includes the following data: ethnicity, geographic origin, age, gender, height, weight, family history, serum ALP, serum phosphate, age at onset, symptoms at onset, history of early cranial suture closure, early tooth loss, failure to thrive, bone fractures, deformities, rickets, pain, epileptic seizures, and renal calcification (nephrocalcinosis).

These clinical data, together with the genetic VUS code in the *ALPL* gene, will be transmitted to the study center in a pseudonymized form. The data transfer to the study center is done via a secure password-protected online portal of the JKU research group. Here, it is checked whether the inclusion criteria are met, and if confirmed, the VUS is tested in the laboratory. The result of the variant testing will be entered into a publicly accessible HPP gene variant database. This will also inform yourself, your child, and your physician or geneticist of the outcome of the testing. Very little clinical information (e.g., your child's age at first symptoms of HPP) is published on a database (website) that serves as a reference tool for physicians and geneticists. Data collection is purely descriptive in nature.

No additional visits to the clinic are necessary.

### **3. What is the benefit of participating in the clinical trial?**

It is possible that your child will derive a direct health benefit from participating in this clinical trial. The knowledge gained may have an impact on establishing a diagnosis of HPP in your child. The publication of the variant in the public database will then also help other people who carry your child's variant.

### **4. Are there any risks, complaints and side effects?**

This study is a registry study. No patient is identifiable in the study. This means study participants have no additional risk by participating in this study.

### **5. When will the clinical study be terminated prematurely?**

You may revoke your willingness to participate and withdraw from the clinical study at any time, even without giving a reason, without any disadvantage to you or your child for further medical care.

Your physician will promptly inform you and your child of any new findings that become known regarding this clinical trial (e.g., when your child's variant is updated in the database) that could become material to you and your child.

### **6. Data protection**

In the course of this clinical study, data about you will be collected and processed. A basic distinction must be made between

- 1) those personal data by which a person is directly identifiable (e.g. name, date of birth, address, social security number, image recordings...),
- 2) pseudonymized personal data, i.e. data in which all information that allows direct conclusions to be drawn about the specific person is either removed, replaced by a code (e.g. a number) or (e.g. in the case of image recordings) made unrecognizable. However, despite compliance with these measures, it cannot be completely ruled out that unauthorized re-identification may occur.

- 3) anonymized data for which a traceability to the specific person can be ruled out.

The investigator who sends your pseudonymized data to the study center or other persons involved in your local medical care have access to the data by which you are directly identifiable (see point 1). In addition, authorized representatives of the sponsor, JKU Linz, who are bound to secrecy, as well as representatives of domestic and/or foreign health authorities and ethics committees responsible in each case may have access to this data, insofar as this is necessary or prescribed for the verification of the proper conduct of the clinical study. All persons who have access to this data are subject to the applicable national data protection regulations and/or the EU General Data Protection Regulation (GDPR) when handling the data.

The code that enables the pseudonymized data to be assigned to your person is only kept at your study center.

Data will only be passed on in pseudonymized or anonymized form.

Only the pseudonymized or anonymized data will be used for any publications.

Within the scope of this clinical study, no transfer of data to countries outside the EU (third country) is planned.

Your consent forms the legal basis for the processing of your personal data. You can revoke your consent to the collection and processing of your data at any time without giving reasons. After your revocation, no further data will be collected about you. However, the data collected until the revocation may continue to be processed within the scope of this clinical study.

According to the GDPR, you are generally entitled to the rights of access, rectification, deletion, restriction of processing, data portability and objection, as long as this does not make the objectives of the clinical study impossible or seriously impair them and as long as this is not contradicted by other legal regulations.

The expected duration of the clinical study is 4 years. The duration of the storage of your data beyond the end or discontinuation of the clinical study is regulated by legal provisions.

If you have any questions about the handling of your data in this clinical study, please contact your investigator first. If necessary, he/she can forward your request to the persons responsible for data protection.

Contact details of the data protection officers of the institutions involved in this clinical study:

Data protection officer of the JKU: [datenschutz@jku.at](mailto:datenschutz@jku.at)

Data protection officer of Kepler University Hospital: [datenschutz@oöeg.at](mailto:datenschutz@oöeg.at)

You have the right to lodge a complaint about the handling of your data with the Austrian data protection authority ([www.dsb.gv.at](http://www.dsb.gv.at); e-mail: [dsb@dsb.gv.at](mailto:dsb@dsb.gv.at) ).

**7. Are there any costs for the participants? Is there any reimbursement of costs or compensation?**

Your participation in this clinical study will not result in any additional costs for you, nor will there be any compensation.

**8. Opportunity to discuss further questions**

Your study physician and his or her staff will be happy to answer any further questions you may have in connection with this clinical study. They will also be happy to answer questions regarding your rights as a patient and participant in this clinical trial.

Name of contact person: Dr. Ahmed El-Gazzar

Reachable at all times at: +43 732 2468 8892

Name of contact person: Univ.-Prof. Dr Wolfgang Högler

Constantly reachable under: +43 57680 84-22001

- Contact details for Upper Austria:

- Upper Austrian Patient Representation
- Bahnhofplatz 1
- 4021 Linz
- Phone: (+43 732) 77 20 142 15
- Fax: (+43 732) 77 20 21 43 55
- E-mail: [ppv.post@ooe.gv.at](mailto:ppv.post@ooe.gv.at)

## 9. Informed consent

Name of patient:

Date of Birth:

I consent to my child participating in the clinical study "Functional Testing of Variants of Unclear Significance in the *ALPL* Gene Cause of Hypophosphatasia". I have been informed that I may refuse to participate without adverse consequences, especially for the medical care of my child.

I have been informed by Mrs./Mr. (Dr.med.) ..... in a detailed and comprehensible manner about the clinical study, possible burdens and risks, as well as about the nature, significance and scope of the clinical study and the requirements resulting from it for me. In addition, I have read the text of this patient information and consent form, which comprises a total of five pages. Questions that arose were answered by the investigator in a comprehensible and satisfactory manner. I have had sufficient time to make up my mind. I currently have no further questions.

I will comply with the medical orders required for the conduct of the clinical trial, but I reserve the right to terminate my voluntary participation at any time without incurring any disadvantages, in particular for my medical care.

I expressly consent to the processing of my data collected in the course of this clinical trial as described in the "Data Protection" section of this document.

I have received a copy of this patient information and consent form. The original will remain with the investigator.

.....  
(Date and signature of patient)

.....  
(Date, name and signature of the responsible investigator)

(The patient will receive a signed copy of the patient information and consent form, the original will remain in the investigator's study folder).