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PATIENT INFORMATION SHEET

for patients aged 18 years and older

Prospective Study

IMPACT - Improvement of Motoric Abilities in Patients with Cystinosis

AIM OF THE STUDY

Infantile nephropathic cystinosis is a rare lysosomal storage disorder. In clinical terms, patients display signs of a chronic multi-organ disease. As early as adolescence, patients with this multi-organ disease suffer from muscular weakness, which initially affects the hand muscles.
In this study, we want to investigate whether your strength and endurance can be enhanced through training with a Galileo vibration platform (*Galileo Med 15 for children and Galileo Med 25 TT for adults*) or Galileo vibration dumbbell (*Galileo Mano Med 20 dumbbell for children and Galileo Mano Med 30 dumbbell for adults*) at home. The overall aim is to positively influence the musculature and cardiorespiratory endurance through physical training in order to avoid medical interventions (corrective surgeries such as correction of the leg axes and feet deformities, conservative therapies such as ortheses and corsets) in the long term and to enhance the quality of life.

Why have you been selected?

You have been chosen because you have infantile nephropathic cystinosis and there are no contraindications for participation.

How is it determined what training my I will do?

As part of the study, participants will be randomized. This means that one half of the patients will exercise at home with the vibration platforms (intervention group) while the other half exercises with hand vibration devices during this time (control group). The decision as to which group you are assigned to is made by Prof. Boulesteix (IBE, LMU Munich) with the help of a computer program. At the end of the study (after 1 year), all participants from the control group will have the

opportunity to train with the Galileo platform and all participants from the training group will be given the chance to train with the hand vibration devices.

How is the study conducted?
Participation in the study involves the following steps:

Initial examination:

- Examination during the interdisciplinary Cystinosis Clinic in Rosenheim (one-day examination)
- Determination of bone-specific parameters
- Cardiology assessment using speckle tracking echocardiography
- Measurement of muscle strength and balance with the Leonardo jumping platform
- Assessment of endurance using the 6-minute walking test
- Measurement of grip strength in the hands
- Completion of further short tests for strength and balance

The measurements of strength, endurance and balance will last several hours and will take place the day before or after the consultation in the Cystinosis Clinic.

Repeat examinations
The measurements of strength, endurance and balance will be repeated twice every three months. These check-ups will last approximately 3-4 hours and will take place in Frankfurt / Main (near the central station).

Final examination
A fourth examination, which corresponds to the initial examination, is planned after 12 months during the annual Cystinosis Clinic.

What data is collected and processed?
Clinical data from the Cystinosis Clinic
At the beginning and end of the study, a clinical examination will take place during the interdisciplinary Cystinosis Clinic in Rosenheim. The doctor will record your weight and height and will ask questions about medication and any further existing diseases. In addition, there will be examinations in different disciplines, including paediatric and/or adult nephrology, pulmonology, endocrinology, logopaedics, neurology and cardiology. The regular ultrasound scans of the thyroid gland and abdomen and a pQCT (XCT 2000) to determine the bone status will also be performed here. These examinations are not specific to this study but part of the regular assessment for monitoring the course of the disease. The doctor will take blood samples to analyse several laboratory parameters, as part of the study. The existing blood sample will be used to determine the laboratory parameters for tartrate-resistant acid phosphatase 5b (TRAP5b), osteocalcin and ICTP (carboxyterminal telopeptide of type I collagen). The electronic data of the pQCT measurement is read out by the manufacturer (Novotec), evaluated and transferred to the Cystinosis Foundation. The data from the clinical examinations is recorded on questionnaires, pseudonymized and forwarded to the IBE, the evaluating institute.

Additional physiotherapy and psychology data
In addition, a physiotherapist will assess your handedness, posture, thoracic mobility and the shape of your spine, leg axis and feet on four different occasions. The muscle strength, endurance and balance will also be measured. The Leonardo jumping platform will be used to measure the bounce and balance through various exercises. Using the walking test, where you have to walk fast for 6 minutes, the endurance is measured. The strength in the hands, which is assessed as grip strength, will also be checked; moreover, we will be performing several other short tests for

strength and balance. During the appointments you will also receive printed psychological questionnaires to assess quality of life and well-being as well as your individual lifestyle. The physiotherapy and psychology questionnaires will be pseudonymized and forwarded to the IBE for data entry.

Access to your health record

By agreeing to take part in this study, you give us permission to access relevant information regarding your health from the patient file of the interdisciplinary Cystinosis Clinic. This includes details on disease symptoms, laboratory results and diagnostic findings (e.g. X-ray, ultrasound, ophthalmologist) as well as clinical or physiotherapeutical treatment data. We will only process data that is required to conduct this study. This data will solely be used for the purpose of this study, any further use is excluded.

Home training

Over a period of 14 weeks, you will carry out daily independent training at home. Patients are divided into two equally sized groups. One group will train standing on a Galileo vibration platform (intervention group), the other group (control group) will exercise the arms with a vibration dumbbell (Galileo Mano) while sitting. Both groups will exercise according to a fixed training schedule. At the beginning of the study, you will receive an introduction to training with the vibration devices. The exercises will be filmed so that you can use the videos at home for orientation. There is also a manual with descriptions and illustrations of the exercises. At least once every two weeks, a mandatory phone or video contact involving a standardized questionnaire with the supervising physiotherapist / sports scientist is scheduled to discuss the training routines, any questions and issues and to adjust the training. If necessary, this can also take place more often. You will keep a training diary to document the training at home. After completion of the intervention, these will be sent to the Cystinosis Foundation by the patients where they are pseudonymized and forwarded to the IBE for data collection and evaluation.

What are the possible benefits of taking part?

We assume that you will directly benefit from participating in this study and training regularly with the Galileo devices. You will have more strength and endurance in everyday life and also an enhanced sense of balance. However, it is also possible that there may be no overall benefit.

Are there any risks for me?

Physical risks

Training with the Galileo devices involves the following risks, both for training with the Galileo platforms and the Galileo dumbbells:

Galileo platforms

- Nausea and dizziness due to rapid, short-term drop in blood pressure
- Quick drop in blood sugar levels in diabetics due to high muscular activity
- Itchiness in the stimulated body regions (especially lower legs) due to high muscular activity
- Blistering at contact points with the vibration platform

The side effects nausea, dizziness, drop in blood pressure and itching are usually harmless. They represent signs of a too high intensity of stimulation or of excessive training duration, which can be resolved by regular training with a correspondingly slow increase in intensity in terms of duration and amplitude (foot position). The Galileo platform may cause an increased activation of muscles especially in the lower extremities, which can result in an increased blood flow into this region. This can lead to a short-term drop in blood pressure and dizziness in sensitive users during or shortly after using the Galileo platform. In particular elderly persons or subjects with known hypotension (low blood pressure) should be specifically advised of the possibility of dizziness or drop in blood

pressure in order to avoid falls caused by dizziness. The occurrence of dizziness should not be seen as a contraindication, but rather as a sign of deconditioning. A slow, adjusted increase in the stimulation intensity and training duration can help.

- ➔ To warm up and better prepare for the training, elderly users or people suffering from hypotension (low blood pressure) can train on a bike ergometer or rowing machine directly before using the Galileo platform.
- ➔ In diabetics, rapid hypoglycaemia (drop in blood sugar levels) can occur especially during and after long, tiring training sessions. Always be prepared with glucose!
- ➔ Skin lesions such as blisters or sore spots on the soles of the feet can be avoided by wearing (dry) socks or thin gym shoes. Please note, however, that users should not wear sturdy footwear as this will impact the therapeutic effect and can soil or damage the Galileo platform.

<u>Galileo dumbbells</u>

- Nausea and dizziness due to rapid, short-term drop in blood pressure
- Quick drop in blood sugar levels in diabetics due to high muscular activity
- Itchiness in the stimulated body regions (especially arms and hands) due to high muscular activity
- Blistering at contact points with the vibration dumbbell

The side effects nausea, dizziness, drop in blood pressure and itching are usually harmless. They represent signs of a too high intensity of stimulation or of excessive training duration, which can be resolved by regular training with a correspondingly slow increase in intensity in terms of duration and grip strength. The Galileo dumbbell may cause an increased activation of muscles, which can result in an increased blood flow into this region. This can lead to a short-term drop in blood pressure and dizziness in sensitive users during or shortly after using the Galileo platform. The occurrence of dizziness should not be seen as a contraindication, but rather as a sign of deconditioning. A slow, adjusted increase in the stimulation intensity and training duration can help.

- ➔ In diabetics, rapid hypoglycaemia (drop in blood sugar levels) can occur especially during and after long, tiring training sessions. Always be prepared with glucose!
- ➔ Jewellery such as rings and watches should be removed before training with the Galileo Mano dumbbell in order to avoid injuries (sore spots) and damage.
- ➔ Skin lesions such as blisters or sore spots on the hands and fingers can be avoided by wearing gloves.

You can stop and interrupt the training at any time. In case of side effects please contact the study coordinators immediately to discuss further proceedings. Please make sure to note the side effects in your diary.

<u>Privacy and safety</u>

All data collected in the course of the study by the Cystinosis Foundation will be pseudonymized and recorded in a computer system. For this purpose, the collected data is first transmitted unencrypted to a doctor who is responsible for the study and is obliged to maintain confidentiality. He/she removes all personal data such as the name, age or address, and replaces them with a unique code. This unique code enables us to link the data from the different examinations. Only a doctor who is responsible for the study will be able to link this code with information that can identify you personally. This link is not disclosed to third parties and the information associated with the respective code is stored securely. Other researchers involved in the execution and evaluation of the study only receive pseudonymized information and have no access to your identity. We store the personal data separately from the encoded data and implement strict security measures to

prevent unauthorized access to this data. It is theoretically possible but unlikely that these security measures concerning the computer systems used to store patient-related data may be breached. If this were to happen, you could potentially be identified, which in turn could lead to a violation of your privacy. However, we will do everything possible to protect the confidentiality of your personal data.

What rights do I have regarding my personal data?
The processing of your personal data is based on the European General Data Protection Regulation (GDPR) as well as the Bavarian Data Protection Act (BayDSG). By signing the consent form, you agree that the study doctors and their staff may collect and use your personal data for the purpose of the above-mentioned study. Personal data includes, for example, your name, date of birth and address, as well as information about your health or disease and other personal data which is collected for a specific purpose during the study or follow-up examinations.

As the principal investigator of this study, PD Dr. Hohenfellner, Pettenkoferstraße 10, 83022 Rosenheim, Germany, is the person responsible for data processing in accordance with the European GDPR. The data collected during the study will be stored for a period of ten years and then destroyed.

In the context of data processing, you have a right of access to all personal data relating to you which is held by the study doctors or the sponsor of the study (including a free copy) in accordance with Art. 13 para. 2 lit. b GDPR. You also have the right of rectification of incorrect personal data. Furthermore, you have the right to withdraw your consent to the processing of your personal data at any time; in the event of such revocation you may request the deletion of your personal data. You also have the right of complaint to the Bavarian Data Protection Commissioner as the supervisory regulatory authority regarding data protection:

Der Bayerische Landesbeauftragte für den Datenschutz
Postfach 22 12 19
80502 München, Germany
Phone: +49-(0)89/21 26 72-0
Fax: +49-(0)89/21 26 72-50
E-Mail: poststelle@datenschutz-bayern.de

Am I insured separately while taking part in the study?
In the context of the study, a so-called trial insurance policy for participants and a group accident insurance policy will be provided. Your trial insurance covers possible injuries or other physical damage due to participation in the study as well as the event of death. The insurance cover includes any damage to health resulting from procedures used in the study or caused by measures carried out on the insured in relation to the study. Where existing illnesses or other causes contributed to the damage independently of the study, insurance cover is only provided for the corresponding causative contribution of the study. The maximum cover for an individual insured person is 250.000,00 Euro, the maximum cover for all claims is 5.000.000,00 Euro.
The accident insurance covers the days on which you attend any of the four appointments in total and includes both you and accompanying persons. The insurance cover is valid worldwide during the effectiveness of the contract for accidents of the insured person - on the direct route from the home, workplace or school / university, - on the direct route from the study site back to one of these places and - during the stay at the study site from the time of entering the site (private practice, study room in a hospital, etc.) until leaving the study site, provided that the study site is visited for the purpose of participation in the study. This insurance cover does not apply if the normal duration of the journey is extended or the journey itself is interrupted by strictly private measures (e.g. attending events, visiting friends or family). The insurance sums per person between the age of 6

and 12 is 5.000,00 Euro for the event of death and 100.000,00 Euro for the event of disability or full invalidity. The insured sums for persons between the age of 13 and 18 are 10.000,00 Euro for the event of death and 100.000,00 Euro for the event of disability or full invalidity. For persons aged 19 to 65 years the insurance sum for the event of death is 50.000,00 Euro and 100.000,00 Euro for the event of disability or full invalidity. We will gladly provide you with the detailed insurance policy conditions on request.

Will the costs be reimbursed?
Travel costs for the introductory training and the check-up appointments are to be paid by the study participants themselves. In urgent cases, financial support for these expenses can be applied for at the Cystinosis Foundation.

Will there be any commercial use of this data?
This study does not pursue any commercial interests. Nevertheless, we cannot rule out that the analysis of the data may result in a recommendation to use Galileo devices for patients with cystinosis. This means that the company manufacturing the Galileo devices could potentially benefit financially.

Will I be paid to participate?
Participation in the study is on a voluntary basis, there is no payment for it.

How can I withdraw my consent to participate in the study?
Participation in the study is completely voluntary. We will only include you in the study if you give your consent. You can revoke your consent to participate in the study at any time without giving reasons and thus withdraw from the study at any time. The withdrawal of consent does not affect your further medical care.
You can withdraw your consent by phone (+49-(0)171 3209639) or by e-mail (heike.holla@cystinose-stiftung.de) and will receive a corresponding confirmation.
If you withdraw your consent, all generate data and any personal details will no longer be used and will be deleted from the database.

Is there a possibility that the study will be discontinued or that I will be excluded from participation in the study?
The principal investigator has the authority to terminate the study at any time or to exclude study participants for safety reasons, if the study protocol is modified or for medical reasons.
These include events listed by the manufacturer as contraindications for training with the Galileo platforms or dumbbells or the need for renal replacement therapy.

Who can I contact if I have questions about the study later on?
As a participant in the study you have the right to contact the principal investigator at any time with questions regarding any aspect of the study.

If you have any questions, please contact us at:
Heike Holla
Case Manager
heike.holla@cystinose-stiftung.de

CONSENT FORM
Patients aged 18 years and older
Prospective Study

IMPACT - Improvement of Motoric Abilities in Patients with Cystinosis

Dr. _____ has given me a detailed explanation of the study "IMPACT - Improvement of Motoric Abilities in Patients with Cystinosis". The consent to take part in this study is on a voluntary basis. If I do not give my consent, my medical care will not be affected. I have received and read the written patient information sheet for patients aged 18 years and older.

I had the opportunity to ask any questions that were important to me and have had these answered satisfactorily.

With my signature I agree that in the context of this study my personal data may be collected, pseudonymized and subsequently shared with third parties. Third parties do not gain access to personal documents; thus, I will not be identifiable to third parties.

I agree to participate in this study and will a receive a copy of this declaration once I have signed it.

STUDY PARTICIPANT

Full name _____

Signature, Date

_____

CONFIRMATION OF THE DOCTOR, Date

_____