UNIVERSITÄTSMEDIZIN GÖTTINGEN UMG

INFORMATION FOR PATIENTS

Information sheet and consent form for an observational study

(European) Alport Therapy Registry-
EARLY PRO-TECT Alport XXL

NCT-number: NCT02378805

Short title: **Alport-XXL**

Version: 1.3, 09.09.2021

Name, address and telephone number of your investigator:

Dear Patient and Dear Relatives/Parents/Guardians

Your consent to participate in an observational study

We would like to invite you to participate in our Europe-wide observational study to protect the kidneys in Alport syndrome.

Background and significance of the observational study

Alport syndrome is a hereditary disease that causes scarring of the kidneys. It can also cause inner ear deafness and eye changes. The kidneys slowly begin to replace healthy tissue by scar tissue early in life and thus lose their function. For the people affected, the disease means a reduction in quality of life. Without treatment, patients need kidney replacement procedures such as dialysis and kidney transplantation often at a young age.

The scarring of the kidney goes through several stages, which the doctor can distinguish. At first, very small amounts of blood can be detected in the urine (microhaematuria). Later, small amounts of the blood protein albumin can also be found in the urine (microalbuminuria), then also other proteins (proteinuria). A blood sample is often needed to determine the exact stage of the disease. However, researchers are working hard to improve knowledge about the course of Alport syndrome and to improve therapy to delay kidney failure.

Monitoring progress of disease in Alport syndrome

Our European Alport Registry was established in 2006 and has already provided very valuable insights that benefit all families with Alport syndrome worldwide: in 2012, we were able to demonstrate that ACE inhibitors in Alport syndrome delay renal failure by years, depending on the early start of therapy (Fig. 1).

Further, we addressed a very important question: Is the start of therapy **before the onset of proteinuria even better and still safe in children**? (blue curve, Fig. 1): The Germany-wide EARLY PRO-TECT Alport study in children aged 2 years and older was able to answer this question in some important aspects: the children were treated with ramipril or placebo (dummy tablet without active ingredient) for up to 6 years at very early stages of the disease. Ramipril was as safe as the placebo tablets. There was clear evidence that ramipril was effective in the very early stages of the disease and delayed the study of the disease. In a strict scientific sense, however, no significance could be shown because of the small number of children included into the randomization arm.

In order to obtain even more certainty for the global treatment recommendation in children in the very early stages, we need long-term follow-up in young patients with Alport syndrome and ask for your help.

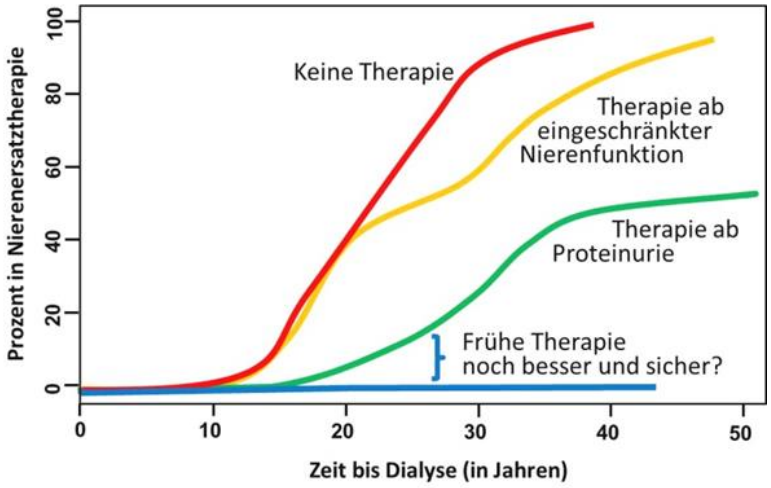

Fig. 1 Protection of the kidneys in Alport syndrome by ACE inhibitors such as ramipril
If **left untreated**, patients with Alport syndrome require dialysis on average in their early 20s (red curve). If treatment is started only when kidney **function is impaired** (yellow curve), kidney failure is delayed a few years. **However, if treatment is** started **from proteinuria** (protein in the urine, green curve), kidney failure can be delayed often by more than ten years.

What benefits can I or other Alport families and doctors gain from participating in the observational study?

There are no direct benefits for you from participating in the observational study. Personally, you cannot expect any direct benefit for your health due to your participation. There is also no risk for you. Your willingness to provide your data for scientific research is a great contribution to help improving our understanding of Alport syndrome and to better and safer treat our young patients.
For the benefit of all patients with Alport syndrome, our follow-up study would therefore like to collect and evaluate your treatment data. This may make it necessary for us to request data already collected from your general practitioner or specialist, with your consent. Even if our register has already improved the treatment of Alport syndrome, there are still many unanswered questions about an even better therapy and its side effects, which need to be investigated further.
The follow-up has no influence on your current therapy.

Implementation of the objectives of the study

Implementation of the goals

This observational study only collects observational data. However, we ask for a common "standard of care" in all patients with Alport syndrome:

1. **The diagnosis of "Alport syndrome" in every patient needs to be confirmed** (e.g. the diagnosis has previously been confirmed by kidney biopsy or by molecular genetic analysis).

2. **Information of the patients or the legal guardians, written consent before passing on the patient data**. Participation is voluntary and can be cancelled by you at any time without giving reasons and without further consequences!

3. The **patient data is recorded pseudonymously**. The patient data from America, Canada, China, France, England, Spain and Germany will be used to compare the treatment worldwide in order to enable international therapy studies with new drugs in the future.

4. **Questionnaire about your particular family history**. Perhaps relatives (e.g. parents, uncles) also have Alport syndrome? This information is very valuable for the quality of the observational study.

5. **Patients under the age of 18 years should be treated by Pediatric nephrologist**, older patients should be treated by adult nephrologist (kidney specialist).

The observational study will only be successful if as many patients as possible participate and the data is collected and made available in full and pseudonymised form. Please help to ensure that in a few years' time further treatment options for patients with Alport syndrome can perhaps be recommended on the basis of clear scientific data.

Participation is voluntary and can be cancelled by you at any time without giving reasons and without consequences!

Personal notes

Contact details test centre

Head of the observational study:

Prof. Oliver Gross, MD
Göttingen University Medical Centre
Clinic for Nephrology and Rheumatology
Robert-Koch-Str. 40
37075 Göttingen
Tel.: 0551-39-60440 / 0551-39-62242 FAX 0551-39-62243
gross.oliver@med.uni-goettingen.de

Data protection

Pseudo-nymisation means encrypted storage of personal data

The use of information about my health is in accordance with legal requirements and needs a written consent before participation. This means that without the following consent, I cannot participate.
During the follow-up, medical findings and personal information will be collected from you and will be documented in your personal file or stored electronically at the study side. Your data is recorded retrospectively and prospectively. This means that your doctor will summarise your previous data on the disease over the past years (retrospective) and also report on how you have progressed with the disease (prospective). The data that are important for the clinical study are also stored in pseudonymised form, evaluated and passed on, if necessary.

Pseudonymised means that no details of names or initials are used, only a number and/or letter code. Only the study doctor at your study centre can decode your data.

The data are secured against unauthorised access. The register has been maintained at the University Medical Centre Göttingen since 2006. Your data will not be forwarded abroad, only a joint evaluation of the data (with foreign countries) will take place.

For details, please refer to the consent form printed at the end of this patient information leaflet.

You will receive a copy of this patient information and the signed consent form. If you have no further questions and have decided to participate in the scientific project, please sign the enclosed consent form.

Declaration of consent

I hereby declare that I am willing to participate in the observational study "European initiative to protect the kidneys in patients with Alport syndrome". I have read the patient information and have been informed verbally about the benefits and risks of the follow-up. I am participating in this follow-up on a voluntary basis. I know that I can withdraw my participation at any time without giving reasons and without consequences. In the event of revocation, I give my consent that the data collected up to that point may be further used for the research project after deletion of the personal data (anonymised).

Test centre *(stamp):*

Investigator:

Name: _____

Phone: _____

Name of the patient in block letters

/ /

Born on (DD/MM/YYYY)

/

Centre - No. / Patients - No.

Signature

Name of the doctor in block letters

I have been informed in detail and in a comprehensible manner by the investigator in a personal consultation about the benefits and risks of the follow-up. I have also read and understood the text of the patient information leaflet (and the data protection declaration printed below). I had the opportunity to talk to the investigator about the study of the follow-up. All my questions were answered satisfactorily.

Possibility to document additional questions from the patient or other aspects of the educational discussion:

I had enough time to make up my mind.

I am aware that I can withdraw my consent to participate in the follow-up at any time and without giving reasons (verbally or in writing) without any disadvantages for my medical treatment.