Trial Description

Title

Early Prospective Therapy Trial to Delay Renal Failure in Children with Alport Syndrome

Trial Acronym

EARLY PRO-TECT Alport

URL of the trial

http://www.alport.de

Brief Summary in Lay Language

Alport syndrome is a hereditary disease which causes renal fibrosis and inevitably leads to end stage renal failure (ESRF). To date, every child diagnosed with Alport syndrome will develop ESRF during the second or third decade of life. No evaluated therapy is available. It is known that ACE inhibitors like Ramipril can slow down reral failure. Today, they are the first line off-label therapy for Alport children with proteinuria for most nephrologist, but they are not authorised for the use in children with proteinuria or any type of renal disease.
In this study, 80 Alport children will receive either the ACEi Ramipril or a placebo without a drug for 3 years. The study is double-blinded (neither patient or doctor knows the kind of treatment) and randomized. If disease is progressing, patient are unblinded and treatment with Ramipril might be initiated. Up to 40 patients might be treated with Ramipil open label. Among others, this study investigates the time until disease progression and the number of adverse events.

Brief Summary in Scientific Language

For the treatment of children with Alport's syndrom and proteinuria, ACE inhibitors (ACEis) like Ramipril are the first line of off-label treatment for most pediatric nephrologists, although ACEis are not authorized in this indication. The current study is a prospective, multi-centered, double-blinded placebo-controlled phase III pediatric study which investigates efficacy (slowdown of disease progression) and safety of the ACEi Ramipril.
Up to 80 eligible patients with Alport Syndrome stages 0 and I will be randomly assigned at a 1:1 ratio to receive once daily oral Ramipril or placebo for 3 years. Randomised patients who progress to the next disease level during the 3-year treatment period will be unblinded, and Ramipril treatment will be initiated, if applicable. The aim is to treat approximately 40 Alport patients open label with Ramipril, including previously treated as well as untreated patients who, or whose parents/legal guardian refuse randomisation after eligibility is confirmed. All patients will undergo study specific procedures according to the study schedule without regard to treatment/ randomisation.

Do you plan to share individual participant data with other researchers?

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[---]*

Description IPD sharing plan

[---]*

Organizational Data

- DRKS-ID: **DRKS00003624**
- Date of Registration in DRKS: **2012/03/23**
- Date of Registration in Partner Registry or other Primary Registry: **2011/12/02**
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **11/6/11 , Ethik-Kommission der Medizinischen Fakultät der Georg-August-Universität Göttingen**

Secondary IDs

- EudraCT-Number: **2010-024300-10**
- Primary Registry-ID: **NCT01485978 (clinicaltrials.gov)**
- BfArM-No.: **4037872**

Health condition or Problem studied

- MedDRA: **10001843 (Alport`s syndrome)**
- ICD10: **Q87.8 - Other specified congenital malformation syndromes, not elsewhere classified**

Interventions/Observational Groups

- Arm 1: **Delix (Ramipril) 2.5 mg tablets for 3 years. The dose of ramipril will be increased over 12 months from a once daily dose of 1 mg/m² to 6 mg/m². The dose will be increased by 1 mg/m² every 2 months until a maximum maintenance dose of 6 mg/m² or the individual MTD is reached. The maximal dose of adults is 10 mg/m².**
- Arm 2: **same number of placebo tablets to Ramipril.**
- Arm 3: **Open label treatment with Ramipril according to the study protocol: Delix (Ramipril) 2.5 mg tablets for 3 years. The dose of ramipril will be increased over 12 months from a once daily dose of 1 mg/m² to 6 mg/m². The dose will be increased by 1 mg/m² every 2 months until a maximum**

maintenance dose of 6 mg/m² or the individual MTD is reached. The maximal dose of adults is 10 mg/m².

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **Double or multiple blind**
- Who is blinded: **[---]***
- Control: **Placebo**
- Purpose: **Treatment**
- Assignment: **Parallel**
- Phase: **III**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **Yes**

Primary Outcome

Primary Efficacy Endpoint: Time to progression of Alport Syndrome to the next disease level within 3 years under ramipril treatment compared to placebo, for all randomised patients.

Primary Safety Endpoint: Incidence of adverse drug events (ADEs, e.g., angioedema, acute renal failure, hyperkalaemia) under ramipril treatment before disease progression compared to placebo before disease progression, for all randomised patients.

Secondary Outcome

Secondary Efficacy Endpoint: Albuminuria after 3 years corrected for baseline albuminuria for patients randomised to receive ramipril compared to placebo.

Secondary Safety Endpoint: Incidence of ADEs (e.g., angioedema, acute renal failure, hyperkalaemia) during 3 years of treatment for patients randomised to receive ramipril compared to placebo.

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Pädiatrie II, Göttingen**
- University Medical Center **Klinik für Kinderheilkunde II, Essen**
- Medical Center **Clementine Kinderhospital, Frankfurt a.M.**
- University Medical Center **Kinderklinik, Hamburg-Eppendorf**
- University Medical Center **Klinikum für pädiatrische Nieren-, Leber- und Stoffwechselerkrankungen, Hannover**
- University Medical Center **Zentrum für Kinder- und Jugendmedizin, Heidelberg**
- University Medical Center **Klinik und Poliklinik für Kinder- und Jugendmedizin, Köln**
- Medical Center **Klinikum St. Georg, Klinik für Kinder- und Jugendmedizin mit KfH-Nierenzentrum, Leipzig**
- Medical Center **Klinikum Memmingen, Klinik für Kinderheilkunde und Jugendmedizin, Memmingen**
- University Medical Center **Dr. von Haunersches Kinderspital, München**
- University Medical Center **Kinder- und Jugendklinik KfH Nierenzentrum für Kinder und Jugendliche, Rostock**
- University Medical Center **Pädiatrische Nephrologie / KfH Nierenzentrum, Münster**
- University Medical Center **Klinik für Kinder- und Jugendmedizin KfH-Nierenzentrum für Kinder und Jugendliche, Jena**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2012/05/31**
- Target Sample Size: **120**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **24 Months**
- Maximum Age: **17 Years**

Additional Inclusion Criteria

- Definitive diagnosis of Alport syndrome: Kidney biopsy (patient or affected relative/s), and/or mutation analysis (hemizygous X-chromosomal or homozygous autosomal-recessive) and assessment of criteria for clinical diagnosis (haematuria, positive family history regarding kidney diseases, ocular changes, labyrinthine hearing loss)
- Alport syndrome levels 0 or I at screening (microhaematuria without microalbuminuria or microalbuminuria [30-300 mg albumin/gCrea]).
- Aged between ≥24 months and <18 years at screening

- Assent from patient and informed consent from parents/legal guardian

Exclusion criteria

- Uncertain diagnosis or variants of Alport syndrome such as a heterozygous carrier
- Alport syndrome levels II, , III, or IV (albuminuria >300 mg/g Crea, creatinine clearance <60 mL/min, or end stage renal failure [ESRF])
- Known allergies or intolerances to ramipril or related compounds
- Known contraindication for ACEi-therapy
- Additional chronic renal, pulmonary or cardiac diseases
- Pregnancy and lactation

Addresses

■ **Primary Sponsor**

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Sources of Monetary or Material Support

- **Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)**

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Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*