PLEASE NOTE: *This study has been imported from ClinicalTrials.gov without additional data checks.*

Trial Description

Title

European Alport Therapy Registry - European Initiative Towards Delaying Renal Failure in Alport Syndrome: Current and Novel Therapies

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

The hereditary type IV collagen disease Alport syndrome inevitably leads to end-stage renal disease. Currently there are no therapies known to improve outcome. Our non-interventional, observational study investigates, if medications such as ACE-inhibitors can (1) delay time to dialysis and (2) improve life-expectancy within three generations of Alport-families in Europe.

Brief Summary in Scientific Language

Early diagnosis in children with Alport syndrome (AS) with isolated hematuria opens a "window of opportunity" for early intervention. Currently there are no causal therapeutic options which are proven to delay renal failure in AS. ACE-inhibition (ACEi) has been shown to reduce proteinuria in Alport patients and to delay renal failure in Alport-mice suggesting it may be of value as an effective treatment to delay renal failure in humans. To test this we established the European Alport Registry to collect data over several generations of Alport families across Europe. Small children with AS first develop microscopic hematuria, proceeding to microalbuminuria, overt proteinuria, impaired renal function and end up with end stage renal disease. These different steps of disease enabled

us to assess if earlier introduction of ACE-inhibition at earlier degrees of disease is more effective than later therapy in delaying the time to dialysis and improving life-expectancy.

Heterozygous COL4A3/COL4A4 mutations result in the phenotype "familial benign hematuria" or "thin basement membrane nephropathy" (TBMN). Affected subjects typically present with hematuria. Having longtime been regarded as "benign" familial hematuria, those patients might have an increased risk to develop severe renal impairment - comparable to the findings in female XLAS carriers (see above). TBMN is not a rare disease, as at least 1% of the population is affected.

For the first time, the present study compares the risk of renal impairment, end stage renal disease and premature death in between heterozygous carriers of XLAS and of ARAS mutations. Additionally, the nephroprotective effect of RAAS-blockade in patients with heterozygous Alport-mutations is evaluated.

Organizational Data

- DRKS-ID: **DRKS00008809**
- Date of Registration in DRKS: **2015/07/08**
- Date of Registration in Partner Registry or other Primary Registry: **2015/02/26**
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **[---]***
- (leading) Ethics Committee Nr.: **[---]***

Secondary IDs

- Primary Registry-ID: **NCT02378805 (ClinicalTrials.gov)**
- Sponsor-ID: **Alport-UMG2010 (University Hospital Goettingen)**

Health condition or Problem studied

- Free text: **Alport Syndrome**
- Free text: **Hereditary Kidney Disease**
- Free text: **Pediatric Kidney Disease**
- Free text: **Thin Basement Membrane Disease**

- Free text: **Familial Benign Hematuria**
- ICD10: **Q87.8 - Other specified congenital malformation syndromes, not elsewhere classified**
- ICD10: **N05.8 - Unspecified nephritic syndrome; Other**

Interventions/Observational Groups

- Arm 1: **Drug: ACE-inhibitor**
- Arm 2: **Drug: AT1-inhibitor**
- Arm 3: **Drug: HMG-Coenzyme inhibitor (statin)**
- Arm 4: **Drug: Spironolactone**
- Arm 5: **Paricalcitol**

Characteristics

- Study Type: **Non-interventional**
- Study Type Non-Interventional: **Observational study**
- Allocation: **[---]***
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **[---]***
- Purpose: **[---]***
- Assignment: **[---]***
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

- end stage renal disease; time frame: unlimited; Age at onset of end stage renal failure
- life-expectancy; time frame: unlimited; life-expectancy of patients and carriers

Secondary Outcome

- proteinuria after initiation of ACE-inhibitor-therapy; time frame: unlimited
- proportion of patients with a clinical diagnosis of hypertension; time frame: unlimited
- proportion of patients experiencing side effects from ACE-inhibitors; time frame: unlimited; defined as acute renal failure (doubling of serum-creatinine), angioedema, hyperkalemia >5.0 mmol/l, dry cough, symptomatic hypotension (orthostatic collapse) and others, and death from all causes.

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- **University Hospital Goettingen, Goettingen**

Recruitment

- Planned/Actual: **[---]***
- (Anticipated or Actual) Date of First Enrollment: **1995/07/31**
- Target Sample Size: **500**
- Monocenter/Multicenter trial: **[---]***
- National/International: **[---]***

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **no minimum age**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

Inclusion Criteria/ Exclusion Criteria:

The diagnosis of Alport syndrome (AS) was proven by kidney biopsy or mutation analysis (or both). Patients were included if they were affected males with X-linked AS or patients with genetically proven homozygous autosomal AS. Patients were excluded if they did not give informed consent or the diagnosis was suspected but not confirmed.

The diagnosis of the heterozygous status was proven by (1) mutation analysis or (2) kidney biopsy plus genetic consultation for decision in between XLAS or ARAS inheritance (including a conclusive genealogic tree and/or linkage analysis).

Exclusion criteria

Patients were excluded

if they were affected males with XLAS or patients with genetically proven homozygous ARAS.
Patients were excluded if they did not give informed consent or the diagnosis was
suspected but not confirmed or if they donated a kidney (living donor to affected family
member).

Addresses

- **Primary Sponsor**

  University Hospital Goettingen

  Telephone: **[---]***
  Fax: **[---]***
  E-mail: **[---]***
  URL: **[---]***
- **Contact for Scientific Queries**

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- **Collaborator, Other Address**

  Gesellschaft für Pädiatrische Nephrologie

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- **Collaborator, Other Address**

  Deutsche Gesellschaft für Nephrologie

Collaborator, Other Address

Deutsche Gesellschaft für Nephrologie

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URL: **[---]***

- **Collaborator, Other Address**

  Alport Selbsthilfe e.V.

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- **Collaborator, Other Address**

  Association pour l'Information et la Recherche sur les Maladies Rénales Génétiques (AIRG)

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- **Collaborator, Other Address**

  KfH Foundation Preventive Medicine

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Sources of Monetary or Material Support

- **[---]***

  Bitte wenden Sie sich an den Sponsor / Please refer to primary sponsor

  Telephone: **[---]***
  Fax: **[---]***
  E-mail: **[---]***
  URL: **[---]***

Status

- Recruitment Status: **Recruiting ongoing**

- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

- Trial results **Temme J, Kramer A, Jager KJ, Lange K, Peters F, Müller GA, Kramar R, Heaf JG, Finne P, Palsson R, Reisæter AV, Hoitsma AJ, Metcalfe W, Postorino M, Zurriaga O, Santos JP, Ravani P, Jarraya F, Verrina E, Dekker FW, Gross O. Outcomes of male patients with Alport syndrome undergoing renal replacement therapy. Clin J Am Soc Nephrol. 2012 Dec;7(12):1969-76. doi: 10.2215/CJN.02190312. Epub 2012 Sep 20.; 22997344**
- Trial results **Temme J, Peters F, Lange K, Pirson Y, Heidet L, Torra R, Grunfeld JP, Weber M, Licht C, Müller GA, Gross O. Incidence of renal failure and nephroprotection by RAAS inhibition in heterozygous carriers of X-chromosomal and autosomal recessive Alport mutations. Kidney Int. 2012 Apr;81(8):779-83. doi: 10.1038/ki.2011.452. Epub 2012 Jan 11.; 22237748**
- Trial results **Gross O, Licht C, Anders HJ, Hoppe B, Beck B, Tönshoff B, Höcker B, Wygoda S, Ehrich JH, Pape L, Konrad M, Rascher W, Dötsch J, Müller-Wiefel DE, Hoyer P; Study Group Members of the Gesellschaft für Pädiatrische Nephrologie, Knebelmann B, Pirson Y, Grunfeld JP, Niaudet P, Cochat P, Heidet L, Lebbah S, Torra R, Friede T, Lange K, Müller GA, Weber M. Early angiotensin-converting enzyme inhibition in Alport syndrome delays renal failure and improves life expectancy. Kidney Int. 2012 Mar;81(5):494-501. doi: 10.1038/ki.2011.407. Epub 2011 Dec 14.; 22166847**

The parameters in ClinicalTrials.gov and DRKS are not identical. Therefore the data import from ClinicalTrials.gov required adjustments. For full details please see the DRKS FAQs.

- Translation on version: 2

- Last processed date by ClinicalTrials.gov: 2015/06/17

** 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.*