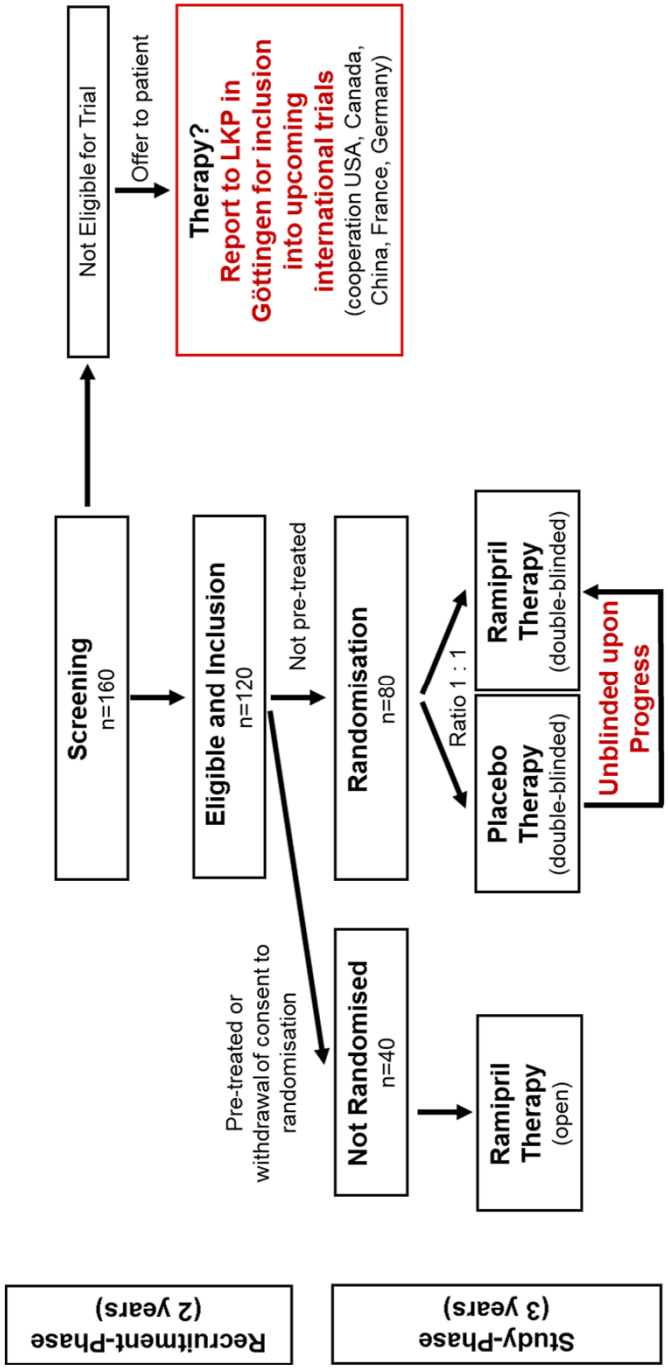

EARLY PRO-TECT Alport - Management

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Hamburg	Prof. Dr. M. Kemper, Universitäts-Kinderklinikum HH-Eppendorf
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Clinical Trial

Version 1.0
for Healthcare Professionals

EARLY PRO-TECT Alport

ACE-inhibitor Ramipril *versus* Placebo in Early Stages of Alport Syndrome: Optimal Start of Therapy and Safety

Start: March 2012

EudraCT-Number:
2010-024300-10

Bundesministerium für Bildung und Forschung

alport selbsthilfe

GPN Gesellschaft für Pädiatrische Nephrologie

Financed by the German Ministry of Education and Research
Supported by the German Alport patient organisation
Supported by the German Society of Pediatric Nephrology

EARLY PRO-TECT

Rationale and Goals

ACE-inhibitors delay renal failure in patients with Alport syndrome [Gross et al, Kidney Int epub 12/2011] if therapy starts after onset of proteinuria (more than 0.3 g/day protein in urine). The goal of this trial is to clarify if an even earlier start of therapy delays renal failure even more effectively and – above all – if therapy at early stages of Alport syndrome is safe.

Design of the Trial

- Prospective, randomized, placebo-controlled, double-blinded, industry-independent, multi-center trial
- Total of 120 patients
- Two years recruitment phase with three years therapy plus six months follow-up per patient

Primary Endpoints

- Progression of renal disease (if renal disease progresses in a placebo-treated patient, the patient will be switched to Ramipril)
- Safety of medication (number and nature of side-effects of Ramipril)

Inclusion Criteria

Patients **aged between ≥24 months and <18 years** at screening**,** with **definitive diagnosis made by:**

- **Kidney biopsy** (patient or affected relative) and/or
- **Mutation analysis** (hemizygote X-chromosomal or homozygous autosomal-recessive)

Normal renal function *plus*

- **Isolated (Micro-)Hematuria** (disease level 0)

or

- **Albuminuria <0.3g/gCrea or <0.3g/day** (disease level I)

or

- **ACE-inhibitor pre-treated patients with Albuminuria <0.3g/gCrea or <0.3g/day**

Main Exclusion Criteria

- Contraindications to ACE-inhibitors
- Uncertain Diagnosis
- Albuminuria >0.3g/gCrea or >0.3g/day; disease levels II, III and IV (Creatinine-clearance <60 ml/min or end stage renal disease)
- Additional systemic diseases

What if the patient has to be excluded from the trial because of proteinuria?

- From mid-March 2012, an NIH-sponsored observational study will be available with participation of the USA, Canada, China, France, and Germany.
- Therefore, **please report every Alport patient to the trial management in Göttingen**, we might be able to offer other international trials to these patients.

Intervention: Medical Therapy

- Ramipril or Placebo starting dose 1 mg/m^2/day p.o. with stepwise increase every two months to the max. tolerated dosage of max. 6 mg/m^2/day
- Every 6 months:
  - Physical examination
  - Laboratory tests
  - Documentation of AEs (and SAEs)
  - Questionnaires to the patients

Secondary Endpoints Sideline Studies

- Proteinuria, decrease of proteinuria
- Creatinine-Clearance
- Height and Weight
- Inner ear hearing defect
- Blood pressure
- Speed of disease-progression

- new diagnostic parameters (urine and serum)
- new prognostic parameters (urine and serum)
- parameters for therapy response