RaDiCo COHORT STUDY INFORMATION SHEET

RaDiCo-ECYSCO

Full title:

European Cystinosis Cohort

Study sponsor: Inserm	**Principal Investigator:** Dr Aude Servais Service de néphrologie adulte AP-HP - Hôpital Necker-Enfants Malades, Paris, FRANCE

Current status of regulatory authorisations

Inserm's sponsorship agreement: 23/06/2015 / **Ethical clearance:** 08/09/2015 / **CCTIRS clearance:** 16/11/2015
CNIL authorisation: 30/09/2016 / **Information System security conformity audit (HADS):** June 2017

Study kick off date	Inclusion period	Follow-up period
12/06/2017	2 years	2 years (min 1 visit/year)

Background and rationale

- Lysosomal storage disease characterized by the abnormal accumulation of the amino acid cysteine. Cystine crystal accumulation in organs causing different symptoms: infantile, juvenile or ocular clinical presentation
- Mutations in the gene CTNS, located on chromosome 17, coding for cystinosin
- Rare autosomal recessive genetic disorder: Incidence 1/180 000 live births - Estimated 140 cases in France and 500-600 in Western Europe
- Significant limitations in the knowledge of natural history and long-term manifestations
- Because of the low incidence of the disease, a European-wide study will be useful to answer the disease related questions
- 2011: Setting up a European observational cohort study by the French National Rare Disease DataBank (BNDMR) using the CEMARA application (13 centres in France and 3 European centres: Italy, Belgium and the Netherlands)
- A switch from the former CEMARA database to RaDiCo is necessary as the cohort needs support to collect, monitor and analyse the data
- In adulthood, care for the cystinosis patients is fragmented with major geographical variability and long term evolution remains unknown
- Project to develop a web-based module in which patients can enter their own data on quality of life
- An active and sustained academic cohort is necessary to avoid independent "drug-oriented" registries, company driven, which would thus lead to a fragmentation of the data

Study type

European multicentre, observational

Objectives

Primary objective

- To understand the natural history and major long-term manifestations and outcomes of cystinosis in paediatric and adult cases

Secondary objectives

- To evaluate the effect of treatment on complications
- To appraise the long-term safety of treatment and compliance
- To evaluate the impact of disease and treatments on patients' quality of life

Improvement of standard care objectives

- To develop comprehensive evidence-based guidelines for treatments, as well as for paediatrics to adulthood, follow-up of patients who will switch from paediatric to adult status

Inclusion and non-inclusion criteria

Inclusion criteria

- Confirmed diagnosis of cystinosis (based on cystine dosage, presence of crystals at eye examination and molecular diagnosis)
- Signed informed consent

Non-inclusion criteria

- Patients not able to give their informed consent.
- No other non-inclusion criteria (patients with associated disease should be enrolled)

Evaluation criteria

Evaluation criteria of the primary endpoint

- Description of complications and variation in the disease course in terms of symptoms:
  - kidney failure: eGFR, renal replacement therapy (RRT) or not and type of RRT
  - Eye symptoms and ophthalmological examination
  - Endocrine manifestations: Pubertal state, hypothyroidism, diabetes mellitus and impaired glucose tolerance
  - neurological abnormalities / muscular manifestations / gastrointestinal manifestations

- Cause of death

Secondary evaluation criteria

- Scores of Quality of Life questionnaires (SF36/SF10)
- Treatment compliance records
- Impact of treatment on frequency and age at complication
- Records of adverse events for the long-term safety

Power

- Considering the context of rare disease and the low number of patients, all available patients willing to participate will be included
- Considering the incidence of the pathology and the number of prevalent patients, the expected sample size is of **400 patients,** of which more than a half will be adult patients

Statistical analysis

- All collected data will be analysed at the end of the 2 years follow-up. The analysis will include survival analysis, description of complications and quality of life.
- The analysis will concern all patients included in the study. All the covariates collected will be described and analysed. The descriptive statistics will concern quantitative and qualitative variables.
- Descriptive analyses will be performed on a yearly basis to identify trends and specific events.

Biocollections

Not applicable

Number of recruiting sites	Prevalent cases retrieved / Inclusion targets vs. current status	
	Year 1	Year 2
France 24, Germany 2, Belgium 1, The Netherlands 1, Italy 1, Spain 1	**207 / 230**	**400**
	207 / 0	-

Public-Private Partnerships valorising the cohort resources

Pending

European valorisation / extension of the cohort

- Besides French patients, the cohort includes Belgian, Dutch, German, Italian and Spanish patients
- Will be a key database within ERKNet, the European Rare Kidney Disease Reference Network (ERN)