Long-term follow-up of nephropathic cystinosis: importance of international registries

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Cohorte RaDiCo ECYSCO

Role of registries

- Help accelerate research
- Provide data necessary to understand the disease course and then to conduct clinical trials
- Improve treatments and outcomes for patients

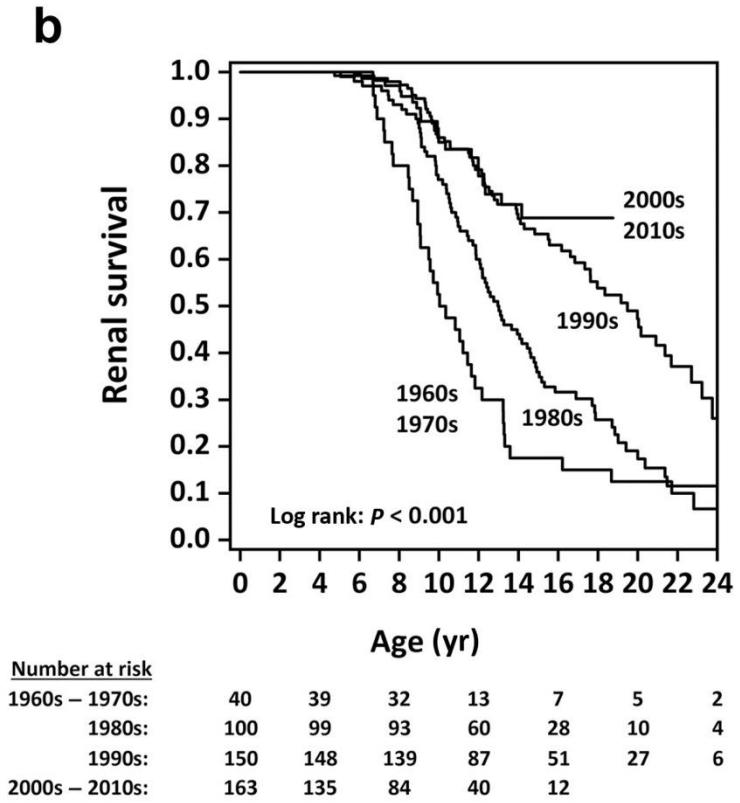
Cure Cystinosis International Registry

IMAGINE WHAT WE CAN DO TOGETHER!

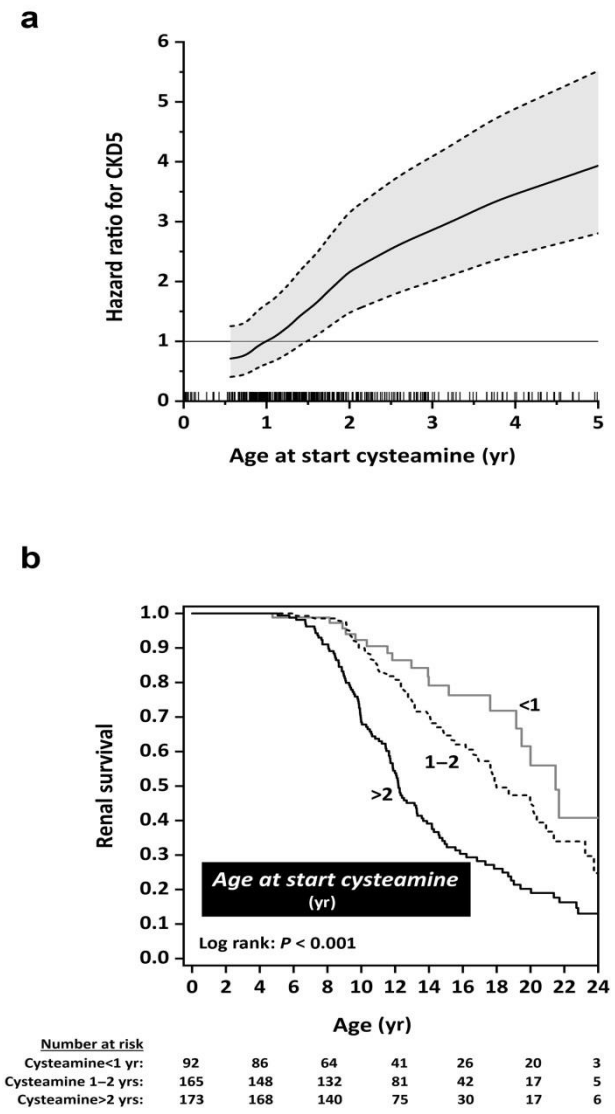
Cure Cystinosis
International Registry

An international cohort study spanning 5 decades

- Data from a large cohort of 453 patients born between 1964 and 2016 and followed in 9 countries
- The prognosis of kidney function has improved steadily between the 1970s and 1990s
- The median gain in renal survival was 9.1 years



- Improved kidney survival was associated with the precocity of treatment with cysteamine and with average leukocyte cystine levels
- By multivariable analysis, the age when cysteamine was started was associated with delayed development of ESRD

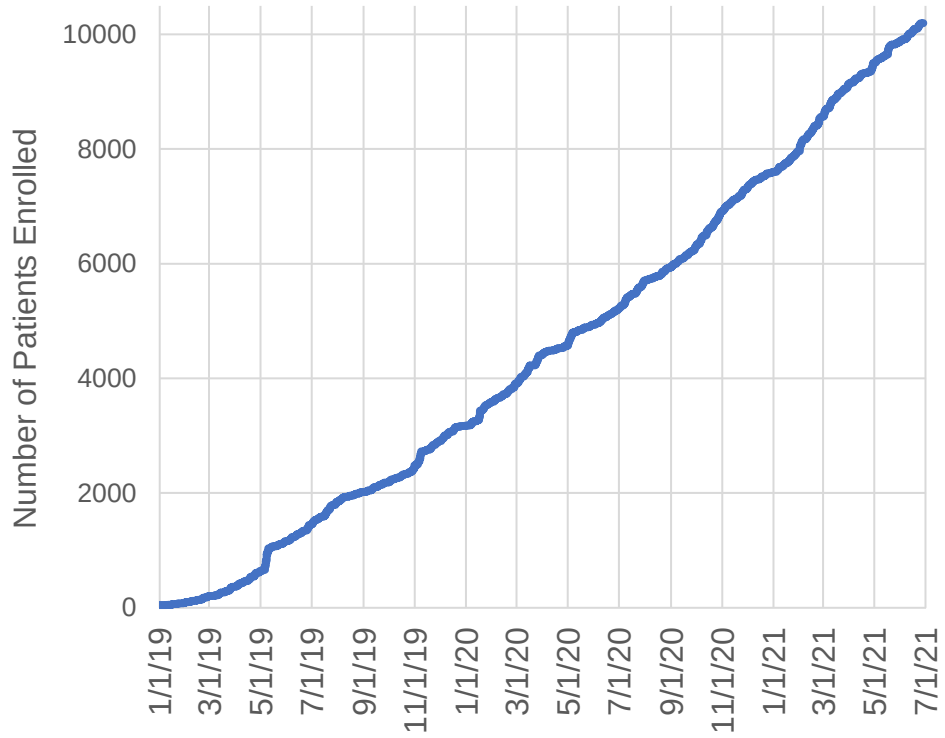


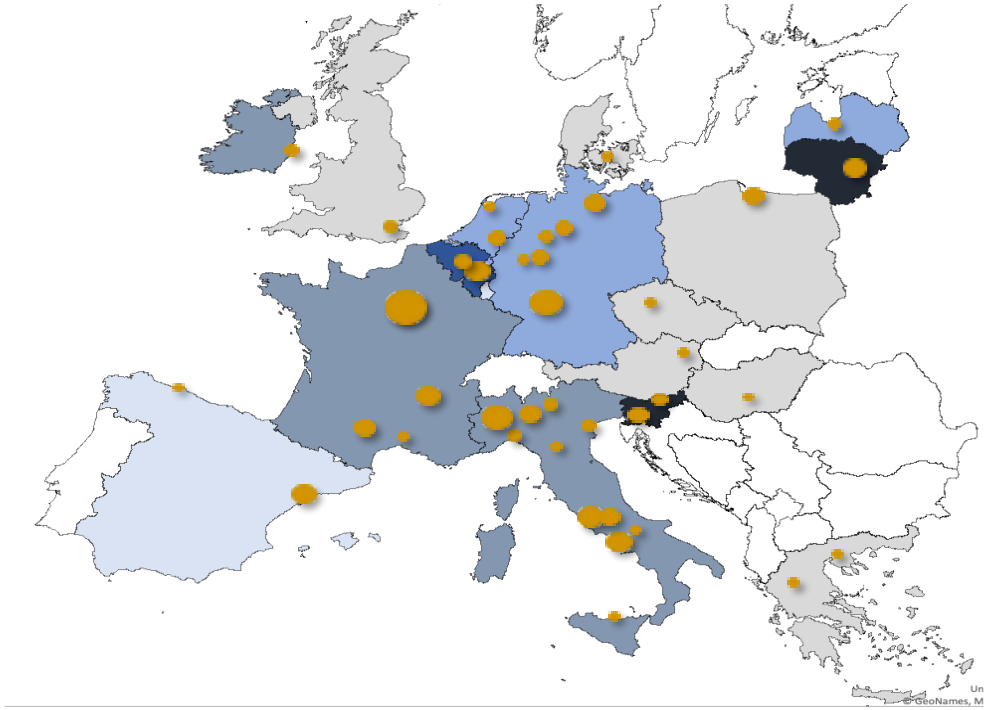
Emma et al, *Kidney Int*, 2021

ERKReg
The European Rare Kidney Disease Registry

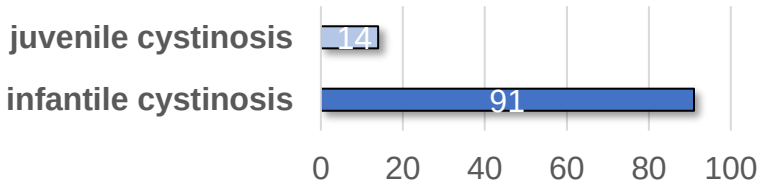
- ERKnet registry (ERKReg): minimal data set

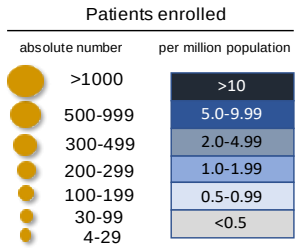
>15 000 patients enrolled





Cystinosis patients in ERKReg
N=105 (seen in 23 ERKReg centers)





RaDiCo program

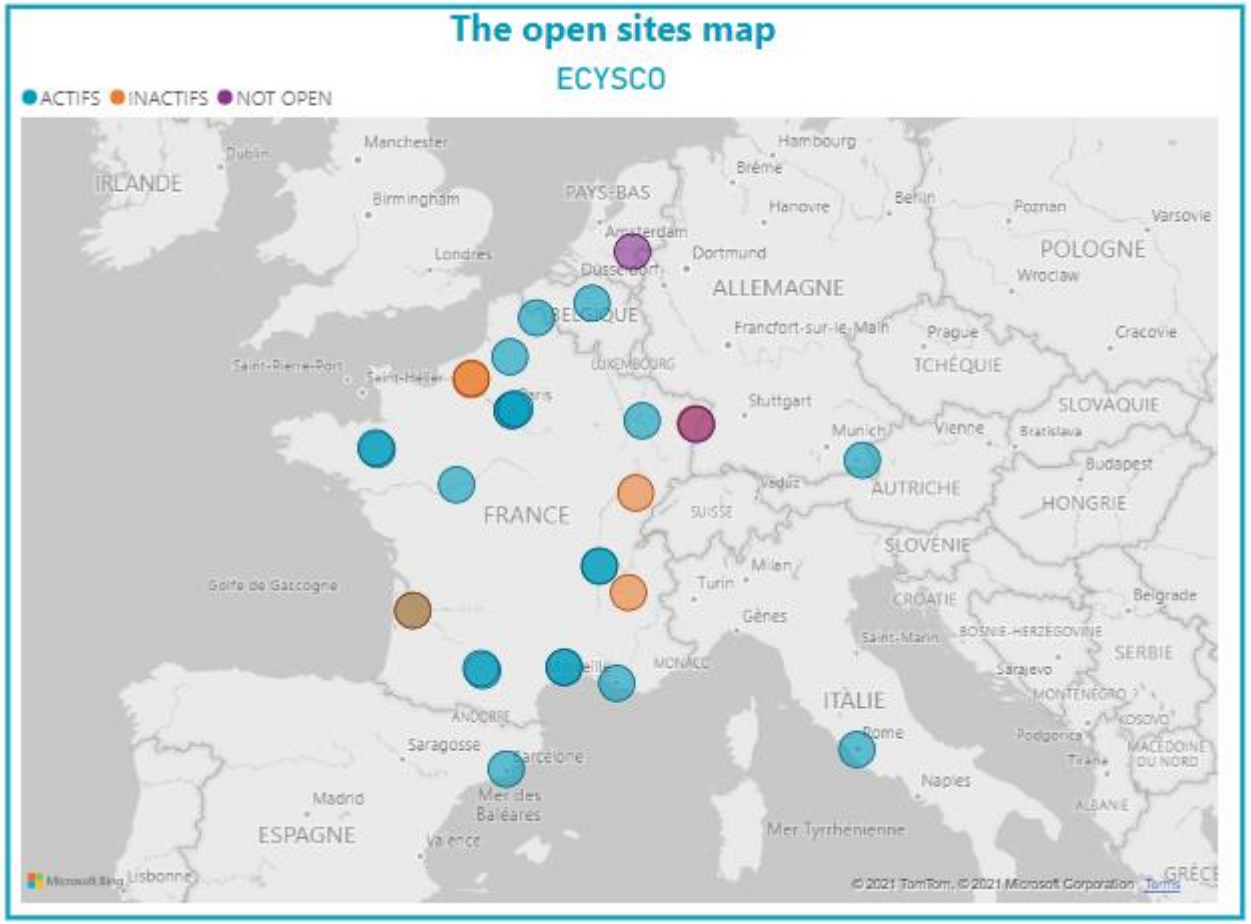
- Funding Entity : French National Research Agency (ANR) - Programme Investments for the future (PIA-1)
- RaDiCo: Expertises and resources organised for collecting, structuring, managing, quality-controlling, analysing data on rare diseases
- RaDiCo objectives:
  - Provide a national and european operational platform
  - Promote and integrate these cohorts in international collaboration
- eCRF: Redcap

ECYSCO European cystinosis cohort: Objective

- ECYSCO is a multicenter longitudinal European cystinosis cohort, retrospective and prospective, from RaDiCo program (Rare Disease Cohort)
- The Primary objective is to describe the natural history of the disease and long-term manifestations
  - Clinical manifestations: renal and extra-renal
  - Treatment
- The Secondary objectives:
  - Evaluate the effect of treatment on complications
  - Define the place for novel therapies
  - Appraise the long-term safety of treatment and compliance
  - Evaluate the impact of disease and treatments on patients' quality of life

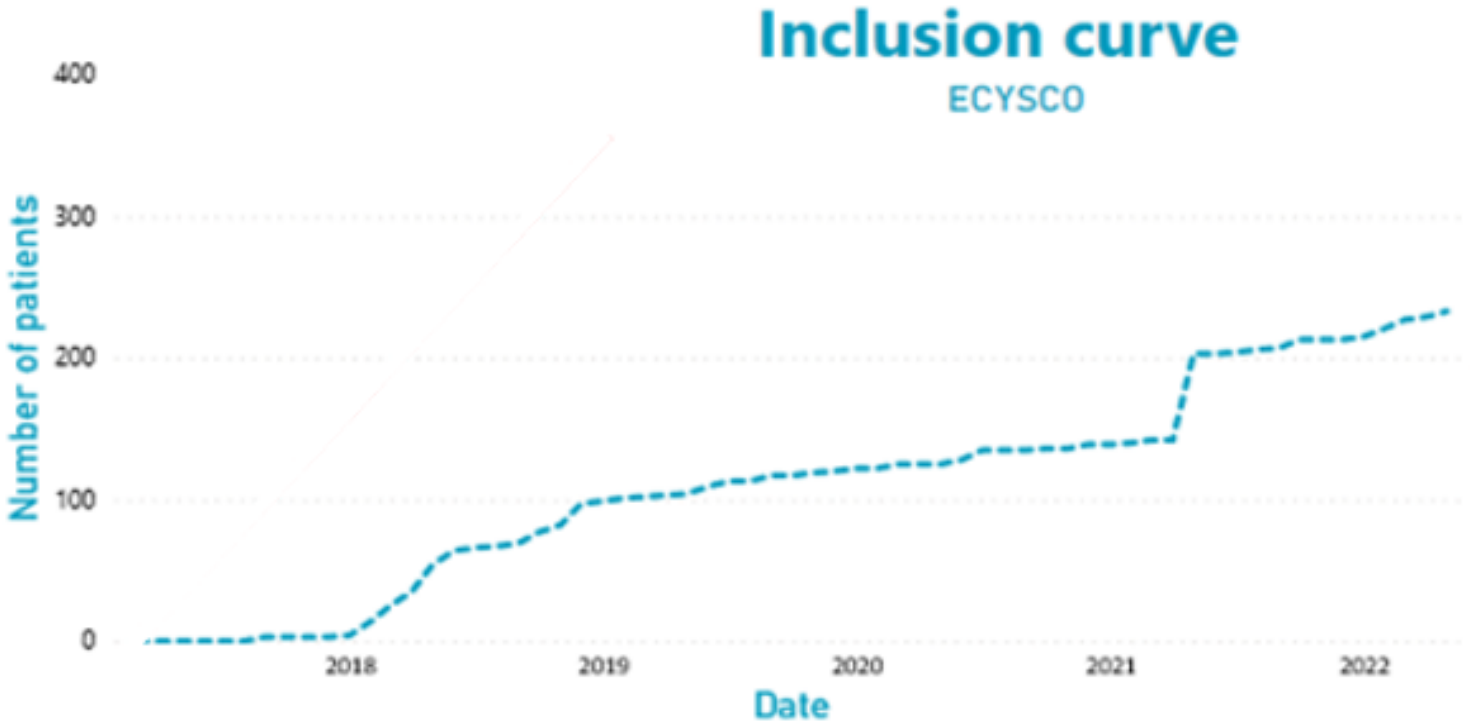
ECYSCO cohort

- Children and adults
- Confirmed diagnosis of cystinosis
- 24 centres in France and 5 centres in other European countries (Rome, Italy; Leuven, Liège, Belgium; Barcelona, Spain; Rosenheim, Germany)

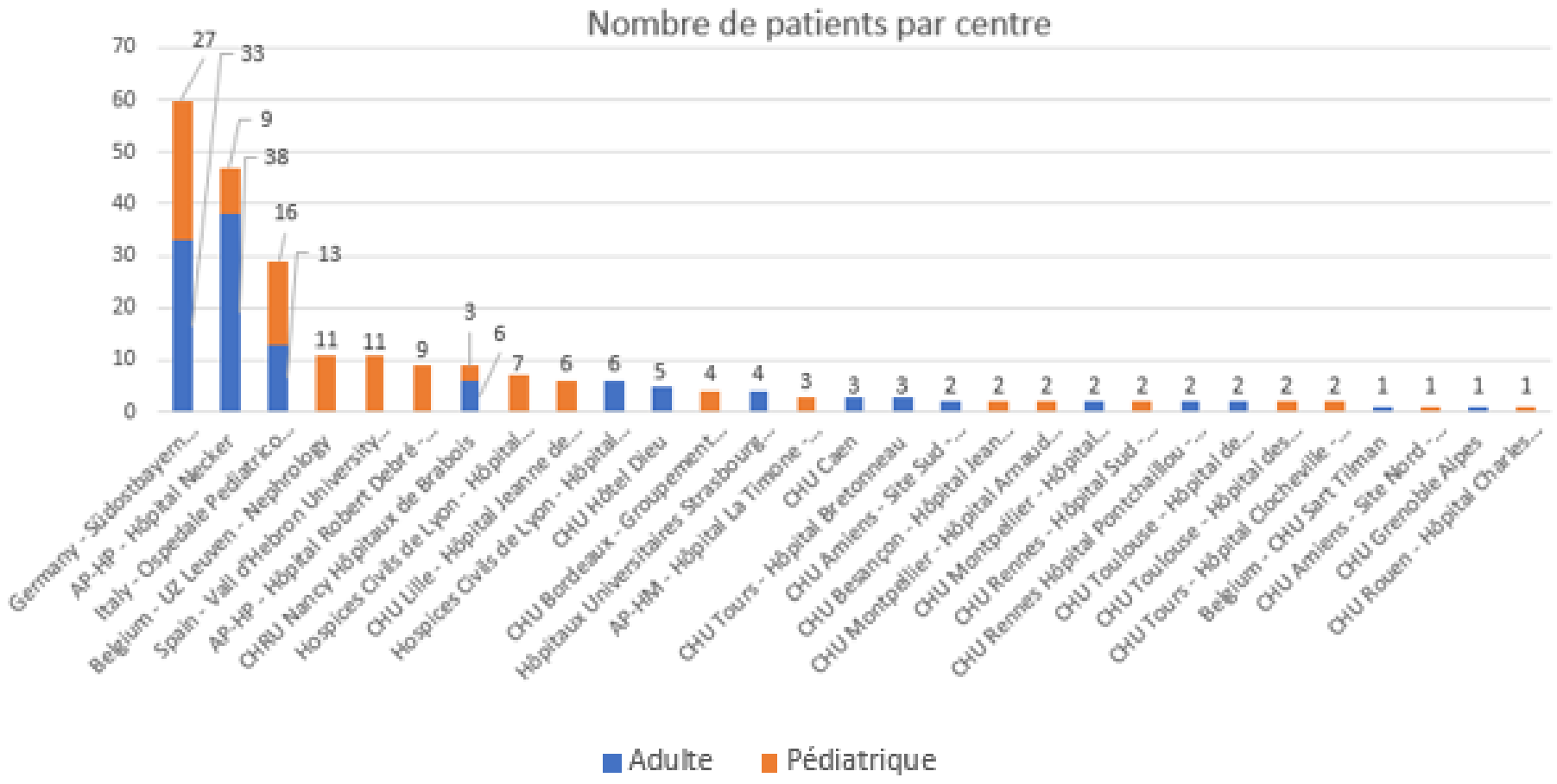


Courbes d'inclusion

Number of recruited patients	Recruitment target at this month	Percentage achieved at this month
239	250	95,6%

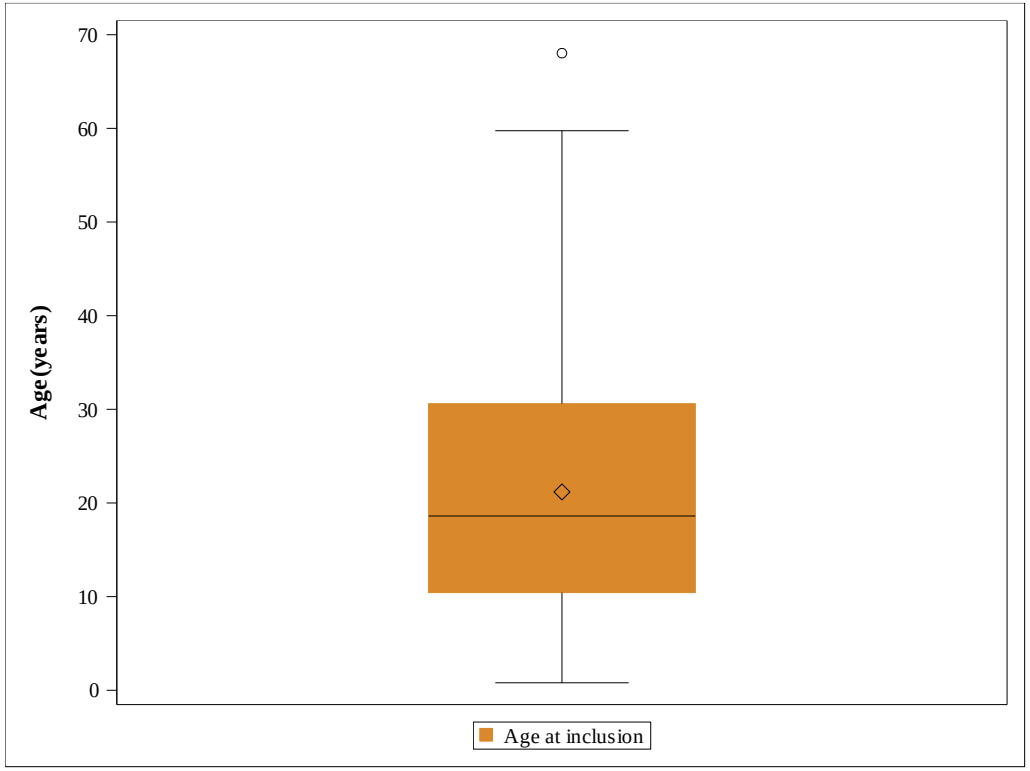


Nombre de patients par centre

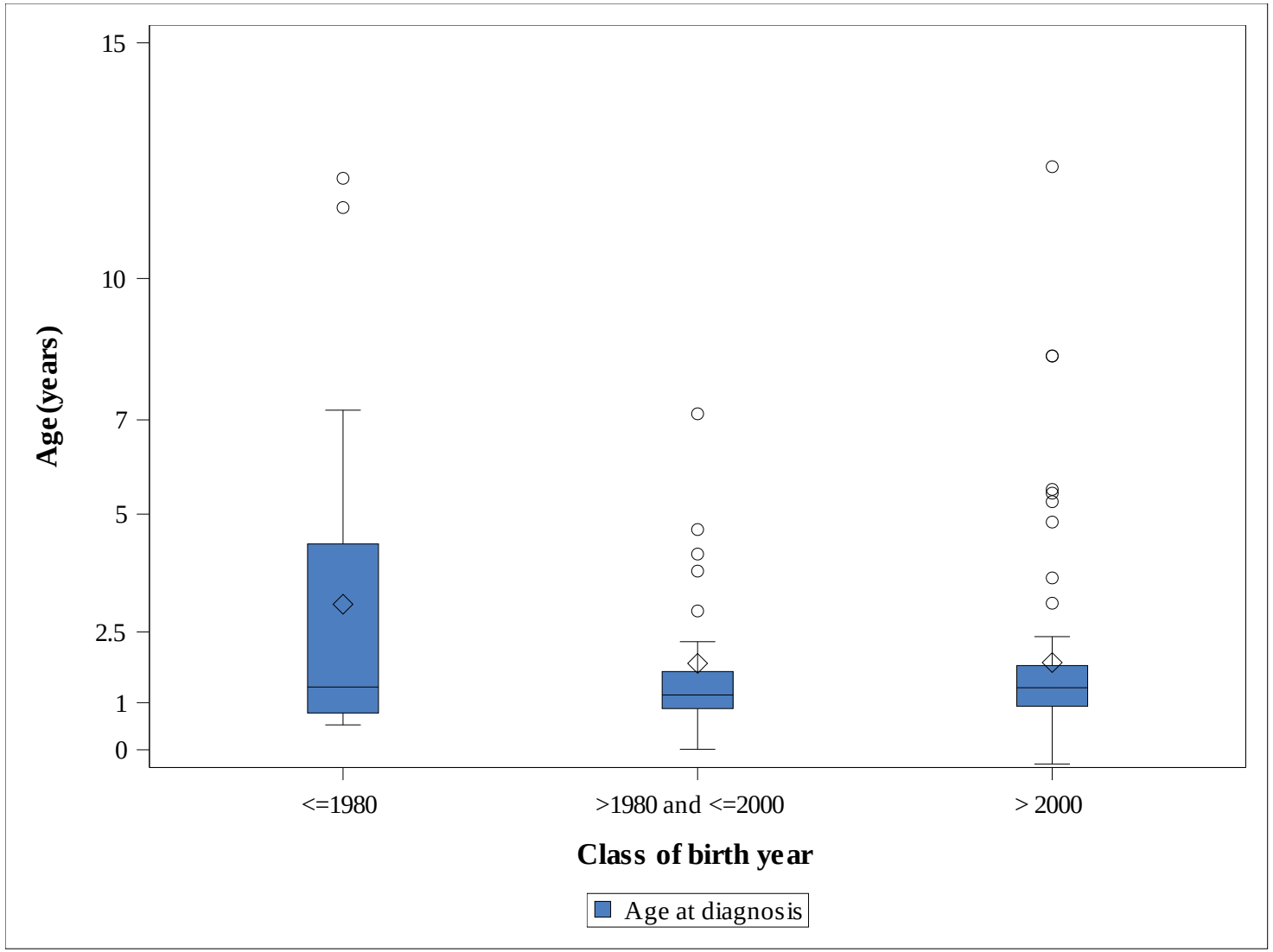


Clinical presentation

N	168
Sex m/f	83 (49%)/85 (51%)
Age at diagnosis (yrs, median)	1,3 (0.90; 1.91)
Age at inclusion (yrs)	18,6 (10.50; 30.64)



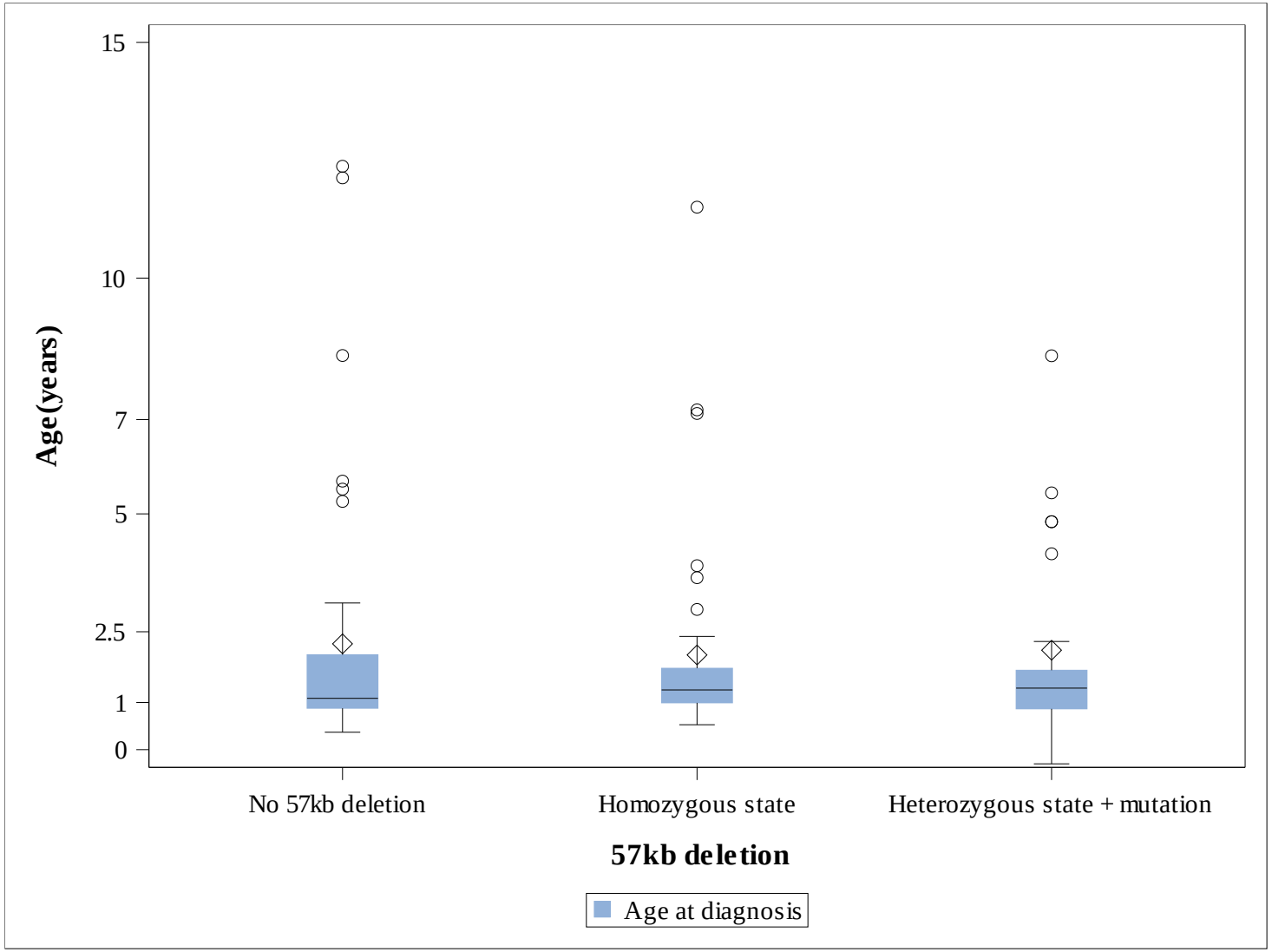
Age at diagnosis



Genetics

- 174 patients had available genetic results
  - 57 (32.8%) homozygous 57kb deletion
  - 71 (40.8%) heterozygous 57kb deletion associated with another mutation
  - 46 (26.4%) other mutations

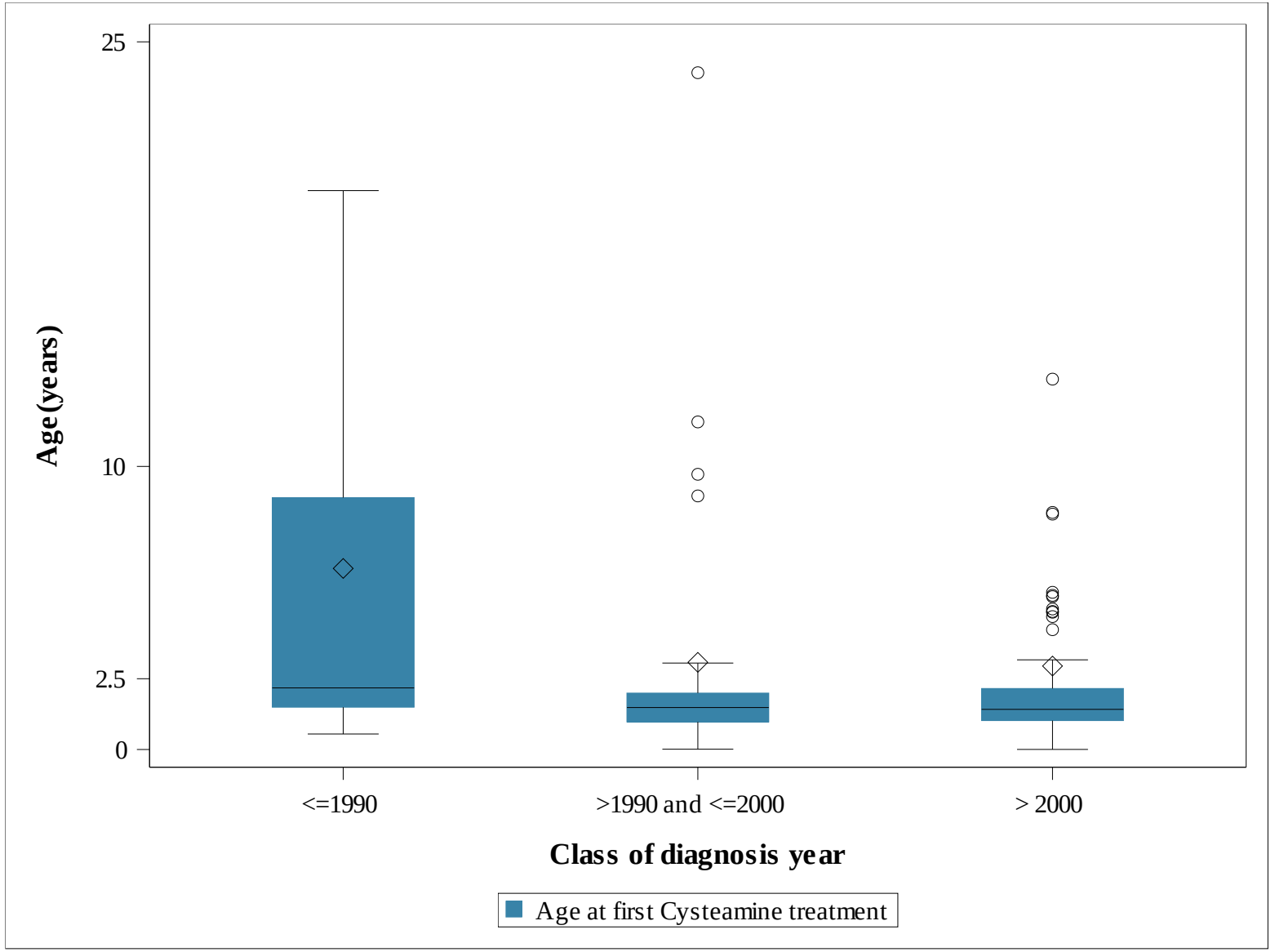
Age at diagnosis according to genetics



Treatment

N	168
Age at cysteamine start (yrs)	1,6 (IQ 1.05-3.01)

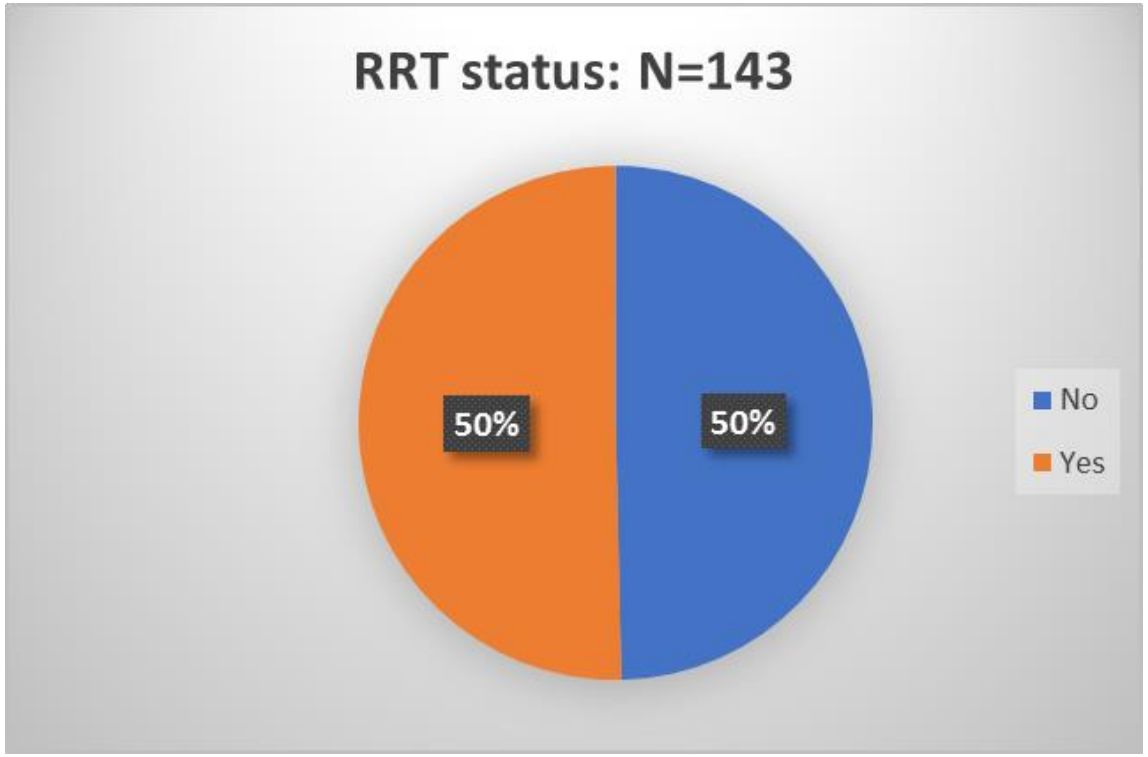
Age at treatment start

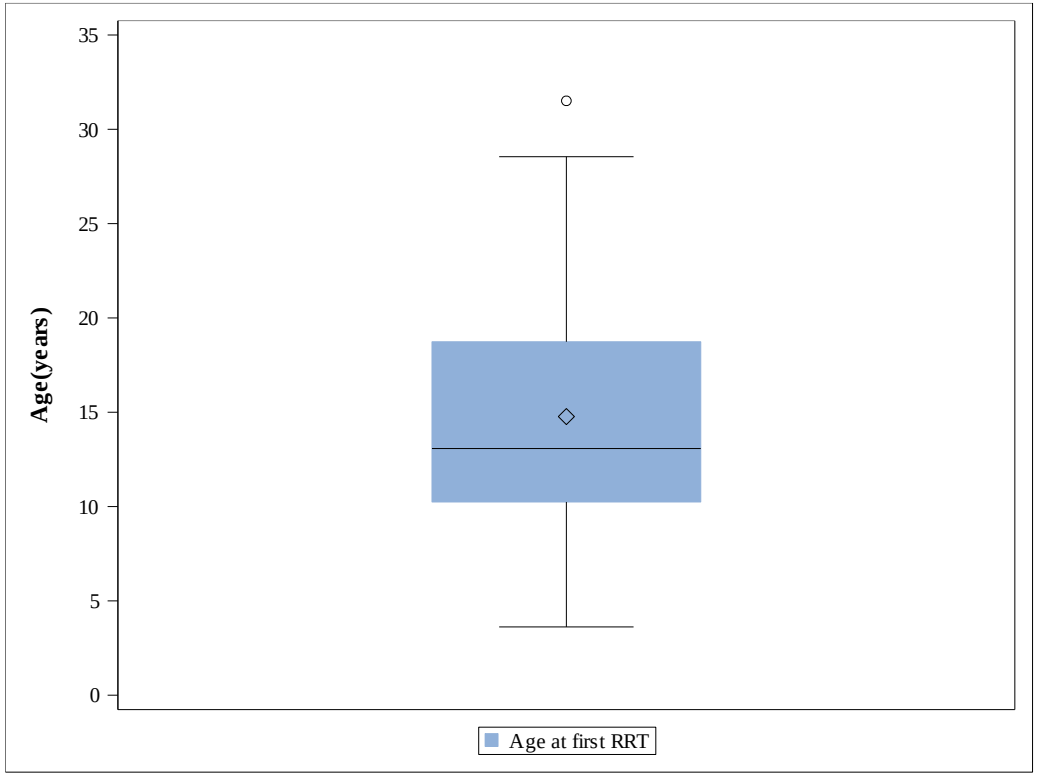


Treatment

N	168
Age at cysteamine start (yrs)	1,6 (IQ 1.05-3.01)
Treatment duration (yrs)	21.6 (IQ 11.90; 31.17)
Cystagon Procysbi	78 90
WBC cystine (nmol ½ cystine/mg)	1,2 (IQ 0.60; 2.10)
Cystadrops®	149 (92,5%)

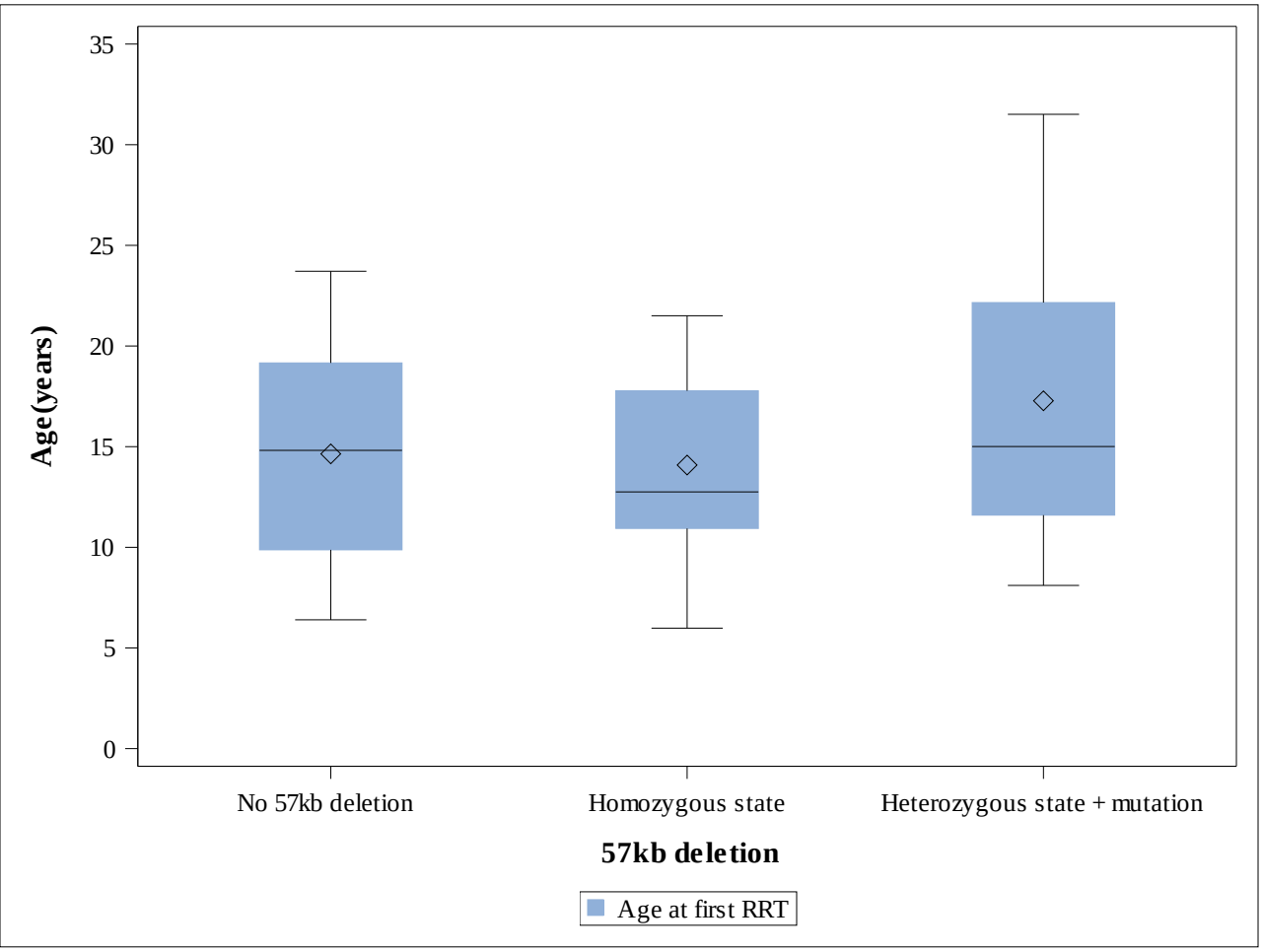
End stage renal disease

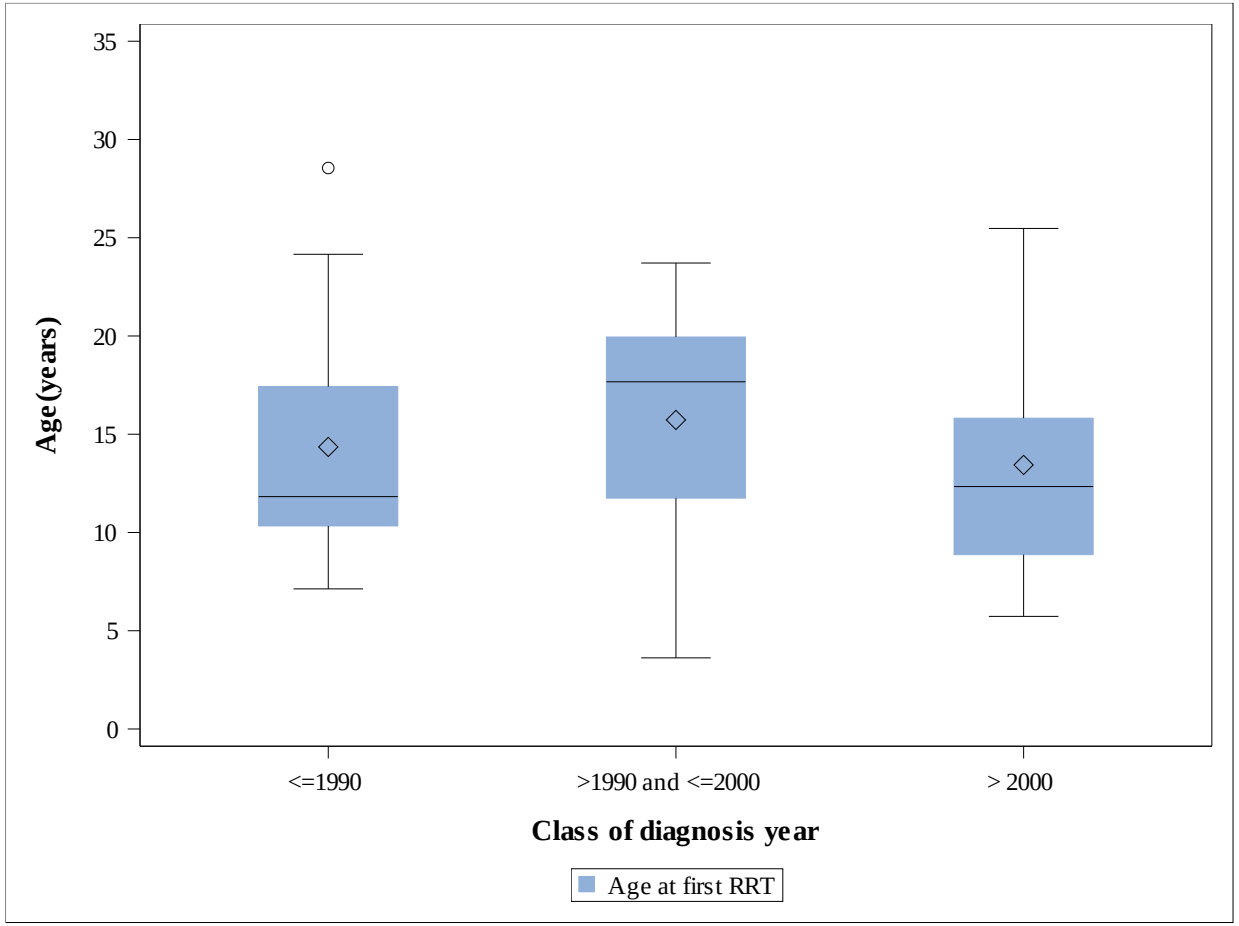




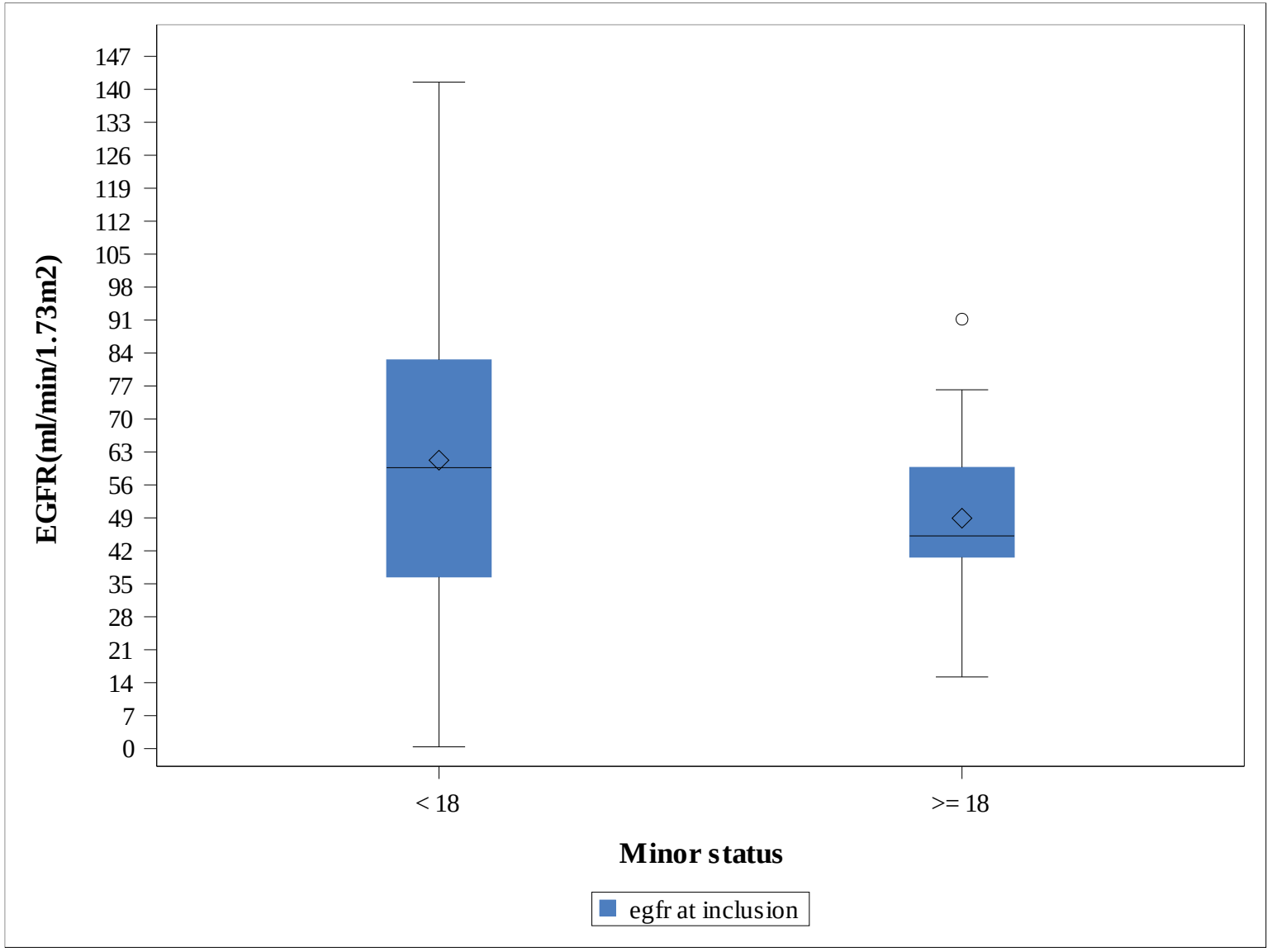
N	143
Age at ESRD (yrs)	12,2 (3,6-31,5)
Number of transplantations	1 (78%), 2 (17%), 3 (4%)

Age at end stage renal disease

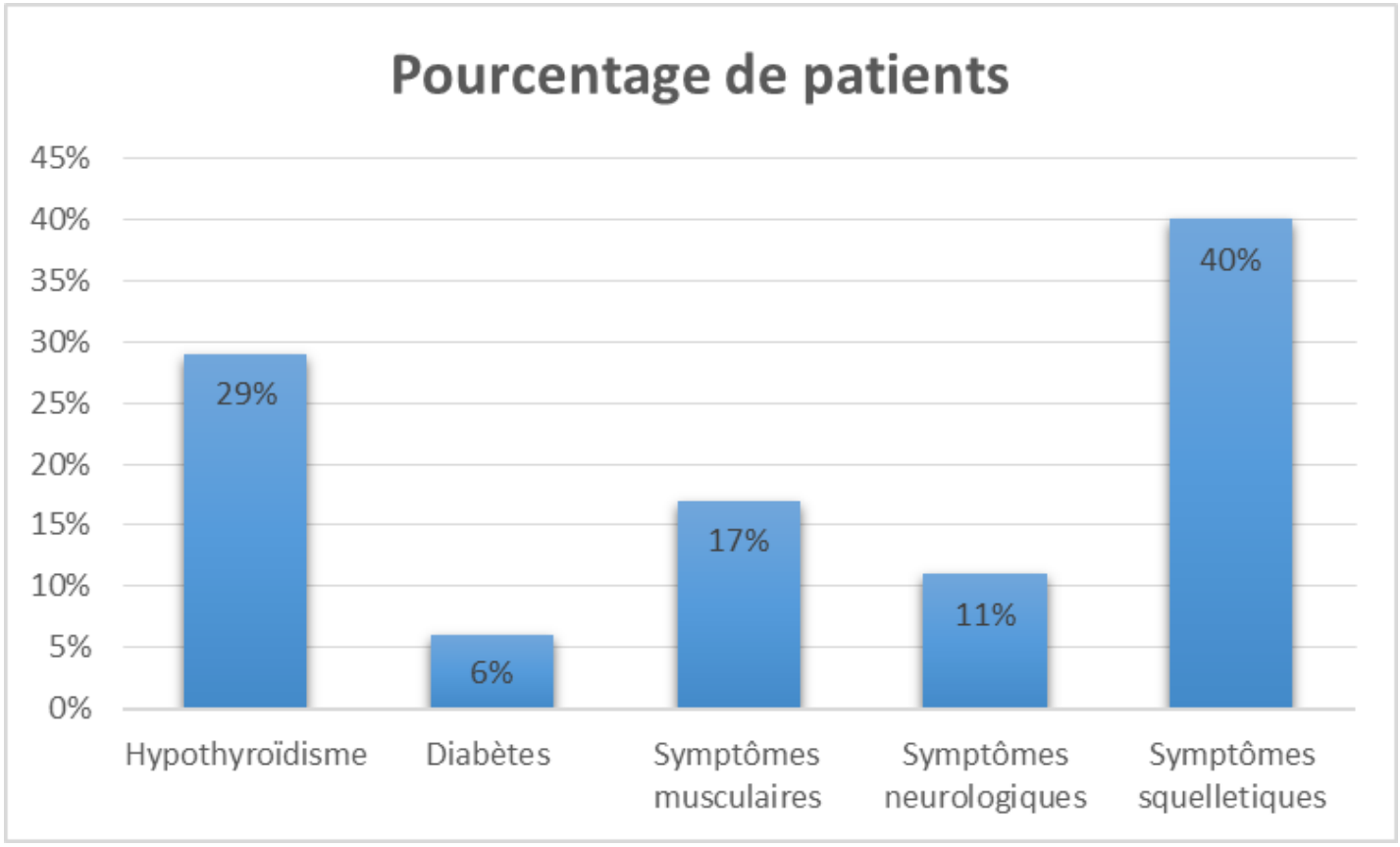


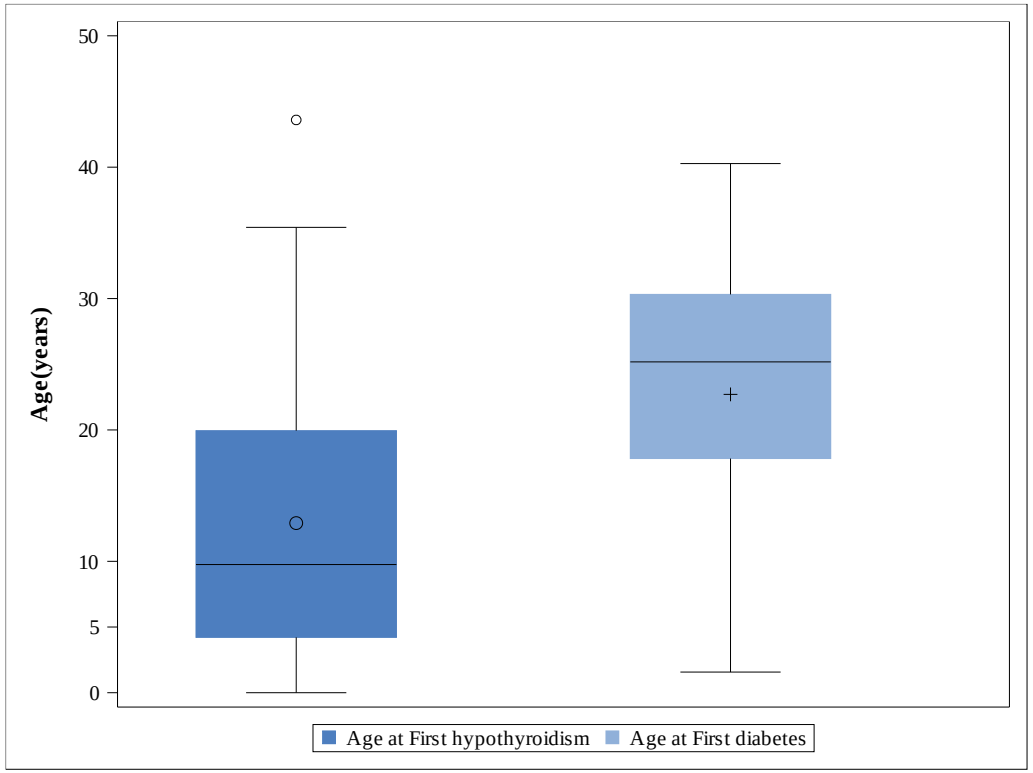


eGFR at inclusion



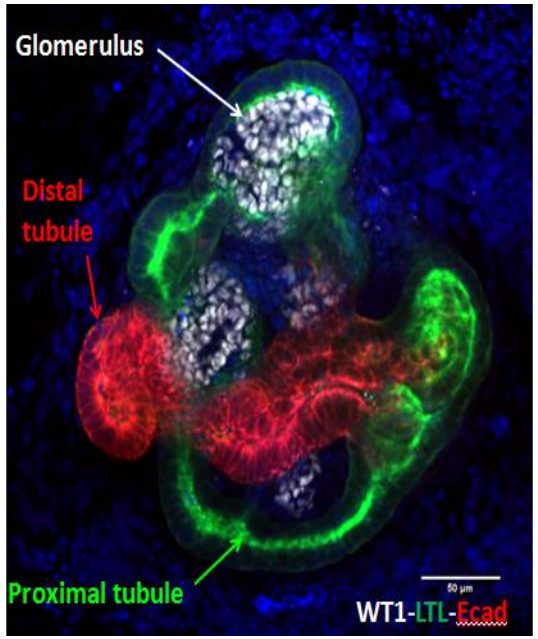
Extra-renal complications





Next steps

- New call of the French National Research Agency : « ANR Maladies rares »
- Follow up
  - to analyse the impact of the treatments on renal function evolution and extra-renal complications
  - to evaluate the impact of the disease and of the treatments on patients' social life and quality of life
- To create a biobank and to identify specific biomarkers
- To develop induced Pluripotent Stem Cells derived from blood cells of patients
- To analyze the mechanisms of bone impairment and to identify putative new therapeutic approaches
- To develop and apply a new quality of life questionnaire



Expected outcomes

- Cohorts contribute to evaluate the effect of the new treatments on the complications of the disease and appraise the long-term safety
  - A well genotyped and phenotyped sustainable quality cohort may be used as a control group and support the identification of patients for future clinical trials
- Diffusion of information, increase standard of care and guidelines
- Cystinosis is a paradigm of a rare disease with active research community allowing the opportunity to dissect new mechanisms of kidney injury

ERKNet

MARHEA
Maladies Rénales Héréditaires de l'Enfant et de l'Adulte

NéphroGones

ORKiD
FILIÈRE ORPHAN KIDNEY DISEASES

- Aude Servais, Necker, Paris
- Patrick Niaudet, Necker, Paris
- Marcella Greco/Francesco Emma, Rome
- Elena Levtchenko, Leuven
- Gema Ariceta, Barcelona
- Georges Deschênes/Julien Hogan, Robert Debré, Paris
- Aurelia Bertholet/Justine Bacchetta, Lyon
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- Robert Novo, Lille
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- Denis Morin, Montpellier
- Dominique Chauveau, Toulouse
- Stéphane Decramer, Toulouse
- Raphael Korman, Nancy
- Noelle Cognard, Strasbourg
- Jacques Dantal, Rennes,
- Jérôme Haranbat, Bordeaux
- Katharina Hohenfellner, Rosenheim

RaDiCo team:

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Isabelle Dufaure-Garé

Serge Amselem

Khalil Bramki

Filière ORKID:

Lamia Toulait

Patients'representative:

François Couppey, AIRG

All the patients