CYSTINOSIS RESEARCH FOUNDATION

GRANT'REPORT
February 20th 2024

Project: Improving characterization of neuromuscular involvement in adults with cystinosis

Recall:

Beside consequences of renal failure, long term prognosis of cystinosis seems to be related to neuromuscular complications. The main manifestations of neuromuscular involvement have been described in previous studies, emphasizing on hand muscle weakness, respiratory insufficiency, and swallowing impairment. However, the long-term consequences and natural history of these symptoms remain an important issue.

We propose to explore thoroughly the neuromuscular complications of cystinosis, focusing on skeletal and respiratory muscles weakness, in a well characterized cohort of patients followed in a French reference center.

Twenty patients will be recruited and evaluated in Garches neuromuscular center in order to assess muscle strength and function with standardized tools. Whole body muscle MRI will be performed in order to better describe the pattern of skeletal muscle involvement. Respiratory muscle damage will be investigated with specific pulmonary function explorations and systematic evaluation of its consequences on breathing efficiency.

We expect with this study to improve the knowledge of neuromuscular manifestations of cystinosis. Increased awareness and characterization of these potentially disabling symptoms should improve care of the patients by leading to a better and more specific management of these complications. This study should also help to identify outcomes measures which could be used in future clinical trials to assess the response of skeletal muscles to innovative therapies.

General Information on the Study:

Objective and primary endpoint:

The main aims of this study are to analyze precisely, with standardized tools in a cohort of adult cystinosis patients:

- The muscle weakness
- The respiratory involvement
- The swallowing function in patients complaining of swallowing difficulties

Objectives and secondary endpoints:

- Evaluation of muscular damage on the radiological level
- Evaluation of lean and fat mass
- Evaluation of sleep disorders
- Evaluation of the evolution of the above-mentioned functions at 12-month intervals

Inclusion criteria:

Cystinosis patients:

- Patient aged from more than 17 years old,
- Patient with confirmed diagnosis of cystinosis,
- Patient with a muscle weakness
- Patient with medical care insurance,
- Patient having dated and signed the Informed Consent Form. If necessary, the information must be given to the legal representative who can be asked to sign/co-sign the Informed Consent Form.

Non-inclusion criteria:

- Refusal to participate
- Patient under AME
- Patient under legal protection
- Pregnant or breastfeeding patient
- Patient that cannot follow the study requirements, for any geographical, social of psychological constraints.

Timeline of the research:

The expected duration of the study is 30 months, with 18 months for inclusion. The data will be collected over 12 months.
Each patients will systematically have:

- muscle evaluation through several physiotherapy scores (manual muscle testing, motor Function Measure, 6 minutes walking test, Handgrip dynamometry and distal motor function)
- muscle imaging by whole-body muscle MRI
- respiratory evaluation through pulmonary function test and transdiaphramatic pressures
- sleep evaluation through a polysomnograpy and capnography
- swallowing evaluation through scores (Salassa and McHorney scores and Sidney swallow questionnaire) and invasive exploration if necessary

Practical procedure:

The study will include a cohort of 20 patients followed-up for 12 months.

Two visits:

- At inclusion (V0)

Reception of the patient in the neurology department of the Raymond Poincare hospital where he/she will have an individual room or a room shared with another patient, 2 days of hospitalization, information and inclusion of the patient, realization of the examinations throughout the 2 days of hospitalization including a recording of the sleep the only night spent in the hospital

- Follow-up visit at 12 months (V2)

Identical organization 1 year later for the second visit. Physiotherapeutic evaluations will require physical manipulations.

Clinical Trial Authorization:

Ethical Committee (Comité de Protection des Personnes):

Submission on June 29th 2022

Approval obtained on July 27th 2022

Patients enrollment:

First patient included and evaluated: September 22th 2022.
Second patient included and evaluated: October 27th 2022
Third patient included and evaluated: October 20th 2022
Fourth patient included and evaluated: November 24th 2022
Fifth patient included and evaluated: January 27th 2023
Sixth patient included and evaluated: April 6th 2023.
Seventh patient included and evaluated: June 15th 2023
Eighth patient included and evaluated: July 3rd 2023
Ninth patient included and evaluated: July 17th 2023
Tenth patient included and evaluated: July 24th 2023
Eleventh patient included and evaluated: July 27th 2023
Twelfth patient included and evaluated: August 31st 2023
Thirteenth patient included and evaluated: September 11th 2023
Fourteenth patient included and evaluated: January 04th 2024

The dates of the next patient inclusions (agreement obtained from patients):
Sixteenth patient: March 3rd 2024
Seventeenth patient: March 21st 2024
Eighteenth patient: March 28th 2024

End of enrollment (recruitment of the 20th patient): planned for May-June 2024.

Patients who completed the study: five

End of study: planned for May-June 2025.

Study documents:

- Protocol
- Informed consent
- Approval of the Ethical committee Comité de Protection des Personnes – IDF III