The organization of care for rare diseases in France: the example of Neuromuscular Diseases

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European Reference Network

Its scope

National Heath Ministry has determined the National Rare Disease actions, and put in place 23 Health networks for rare diseases in 2014 to Coordinate the implementation of NRD in accordance with the stated timetable

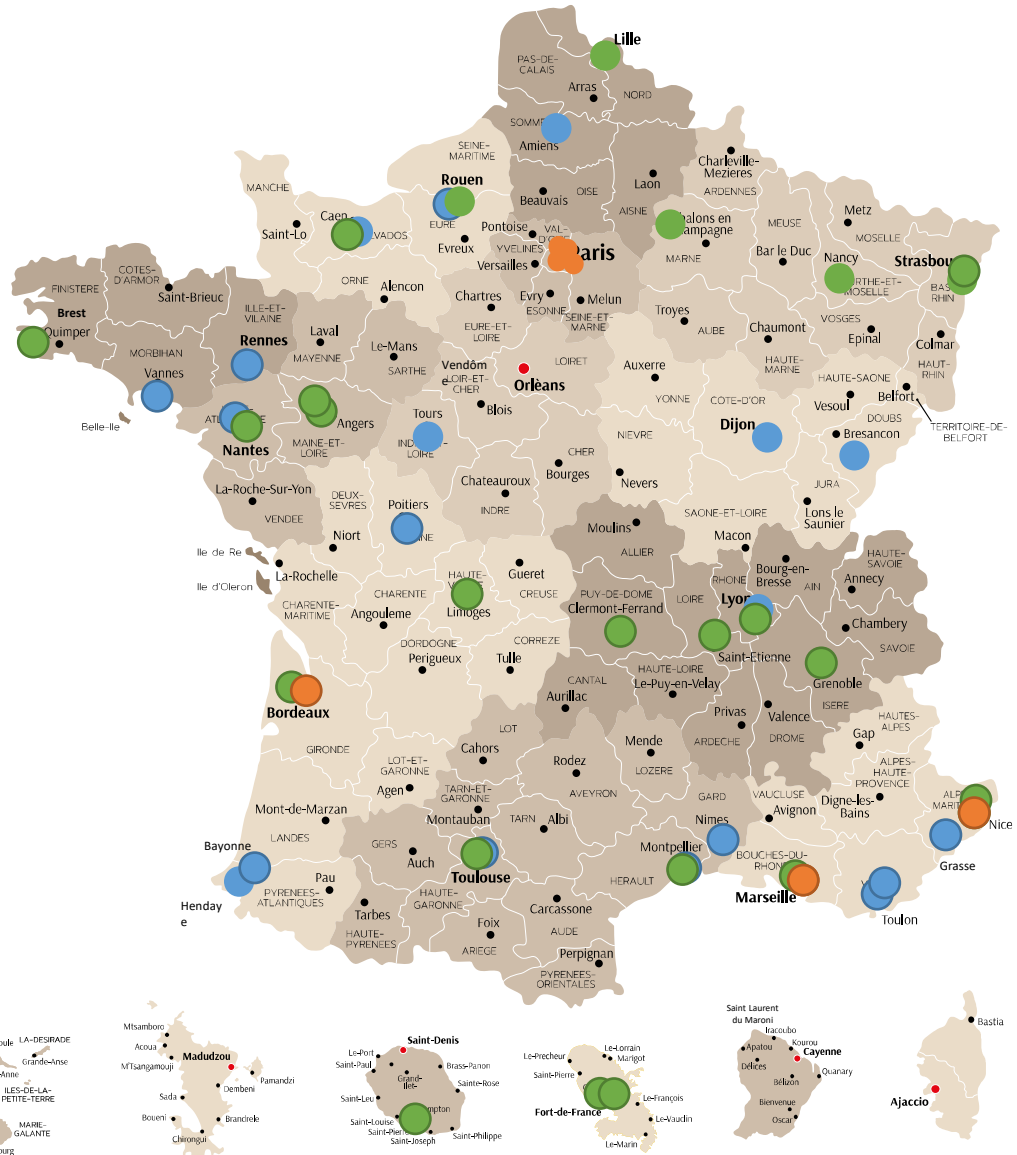
5 axes :

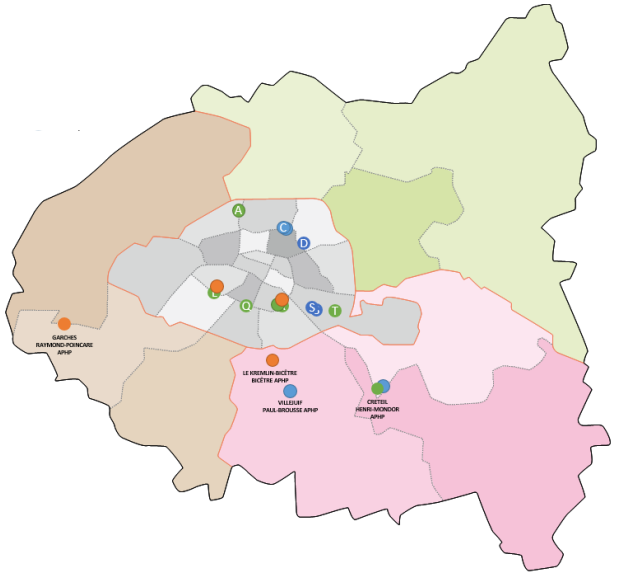
1- Care
2- Training
3- Information
4- Research
5- Europe and International

- Nearly **700** different forms of neuromuscular diseases
- **60 000 Patients** in France .

Filnemus centers in 2023

- Coordonnateur
- Constitutif
- Compétences





Facilitate, promote, enhance, innovate

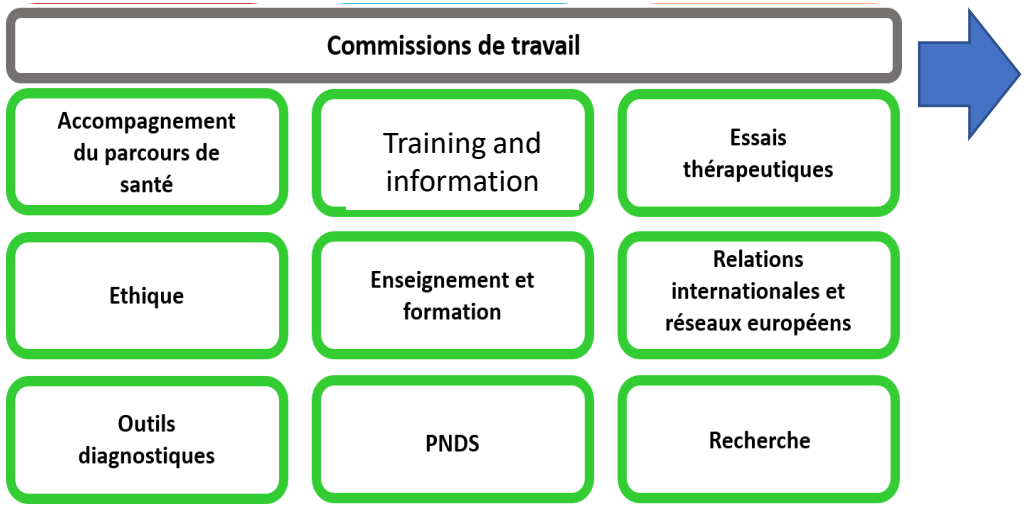
- ✓ **Coordinate the implementation of** the National Rare Disease actions, in accordance with the stated timetable
- ✓ **Stimulate a positive dynamic** among all the members of the network
- ✓ **Helping teams** when they face blockages
- ✓ **Valorize** the teams and valorize the network
- ✓ **Disseminate** important information as widely as possible
- ✓ **Communicate** on the progress of the actions
- ✓ Be the link between the National Heath Ministry and the centers
- ✓ To bring its vision, continuously **innovate**

Allocation of actions to the different commissions

Period 2018-2024

5 axes :

1- Care
2- Training
3- Information
4- Research
5- Europe and International



The actions of the Filnemus

Example of some major actions to improve care

1- Reduce wandering and diagnostic impasse
2- Therapeutic trials and innovative therapies
3- The treatment observatory
4- Organize Multidisciplinary Consultation Meetings (MCM)
5-Therapeutic Education Programs (TEP)
6- National care protocol recommendations
7- Organization of access to very high throughput genomic sequencing platforms
8- Neonatal screening in SMA, DMD
….
….

Online training

Webinars, e-learning modules, podcasts.

10 Webinars in 2023

3rd Thursday of each month

On the Filnemus website in free access in live Then in **replay**

At 6pm live

A specialist speaker on the subject and a moderator

9 e-learning modules

Available on the Filnemus website

40 Podcasts

Available on the Filnemus website

- Amyloidosis
- Diagnostic wandering
- CMT
- SMA
- Myasthenia
- Stif Person sd

Training/ Information Meetings

2018
- → Annual Filnemus meeting
- → Diagnosis for everyone" day

2020
- → Annual Filnemus Day

2022
- → Annual Day
- → ETP Day
- → Pompe disease Day
- → Juvenile Dermatomyositis Day
- → Rhabdomyolysis Day
- → Anatomopathology and Biobanking Day

We organized 16 meetings on different neuromuscular diseases:

2019
- → Annual Day
- → Innovative therapies" day
- → Cognitive impairment day

2021
- → Annual Day
- → Database Day
- → Innovative therapies" day
- → Ethical Reflections Day

2023
- → Annual Day
- → Innovative therapies in CMT" day
- → Wandering diagnostic day
- → Emergency Day
- → Heart/Muscle Day

- → Genetic training
- → JIMI Days

Training/ Information

- **22** recommandations in NM diseases

- **40** Therapeutic Education Programs

- **Directories :**
  - Neuromuscular trainings
  - Professional and patient documentations
  - Therapeutic trials in France

Organize access to very high throughput genomic sequencing platforms

National French Consensus on gene lists using NGS

European Journal of Human Genetics (2019) 27:349–352
https://doi.org/10.1038/s41431-018-0305-1

ESHG

ARTICLE

A National French consensus on gene lists for the diagnosis of myopathies using next-generation sequencing

Martin Krahn[1,2] · Valérie Biancalana[3] · Mathieu Cerino[1,2] · Aurélien Perrin[4,5] · Laurence Michel-Calemard[6] · Juliette Nectoux[7] · France Leturcq[7] · Céline Bouchet-Séraphin[8] · Cécile Acquaviva-Bourdain[9] · Emmanuelle Campana-Salort[1,10] · Annamaria Molon[10] · Jon Andoni Urtizberea[11] · Frédérique Audic[1,10] · Brigitte Chabrol[10] · Jean Pouget[1,10] · Roseline Froissart[9] · Judith Melki[12] · John Rendu[13,14,15] · François Petit[16] · Corinne Métay[17] · Nathalie Seta[8] · Damien Sternberg[17] · Julien Fauré[13,14,15] · Mireille Cossée[4,5]

genes

MDPI

Article

A National French Consensus on Gene List for the Diagnosis of Charcot–Marie–Tooth Disease and Related Disorders Using Next-Generation Sequencing

Thibaut Benquey [1,†], Emmanuelle Pion [2,3,†], Mireille Cossée [3,4,‡], Martin Krahn [5,6,‡], Tanya Stojkovic [7], Aurélien Perrin [4], Mathieu Cerino [5,6], Annamaria Molon [8], Anne-Sophie Lia [9], Corinne Magdelaine [9], Bruno Francou [10,11], Anne Guiochon-Mantel [10,11], Marie-Claire Malinge [12], Eric Leguern [13], Nicolas Lévy [5,6], Shahram Attarian [5,14], Philippe Latour [1] and Nathalie Bonello-Palot [5,6,*]

Filnemus Multidisciplinary consultation meetings

Multidisciplinary consultation meetings available with the dedicated tool

10 National MCMs

- *Innovative therapies "adult spinal muscular atrophies "*
- *Innovative therapies "amyloid neuropathies*
- *Complex autoimmune neuropathies*
- *Pompe Disease*
- *….*

14 MCMs for very high throughput genomic sequencing

- *Neonatal hypotonia of peripheral origin*
- *Undetermined genetic myopathies*
- *Undetermined Mitochondriopathies*

157 MCMs

Organize access to very high throughput sequencing platforms

Pre-indication	Mitochondrial diseases	Neonatal hypotonia	Unlabeled myopathies
Files presented in MCM	176	37	115
Files validated in MCM	90	32	87
Samples sent to platforms	87	30	84
Sequenced samples	63	24	56
Results	18	8	11

To reduce diagnostic wandering and diagnostic impasse

50%

of patients are without a precise diagnosis.

1/4

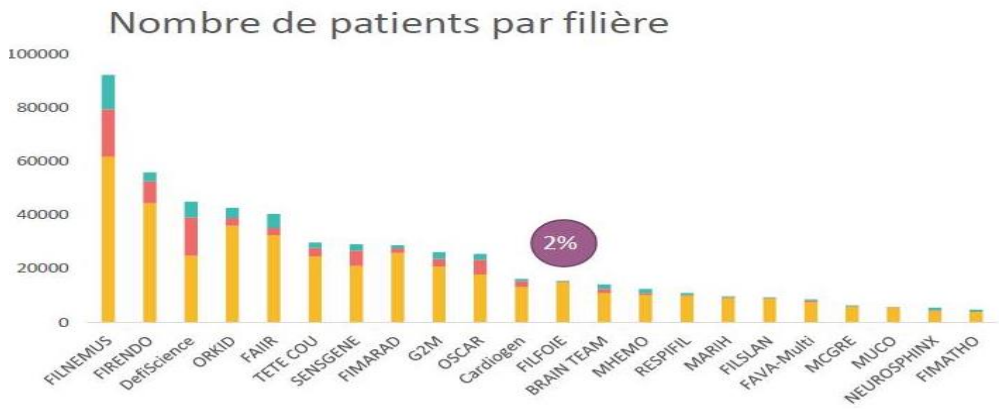
of people with the disease wait **4 years for** a diagnosis to be considered.

1.5 years

This is the time to diagnosis and more than **5 years** for ¼ of people.

BAMARA

BNDMR
Banque Nationale de Données Maladies Rares
bndmr.fr



• Wandering and Diagnostic Impasse Pilot Project

Wandering and dead end project:

Pilot phase

Sep 2020 - June 2021

6 coordinating CRMRs

25 constituent CRMRs

8 CCMR

27 CRAs recruited

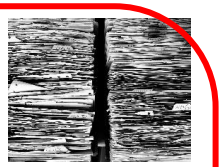
National Coordination

- Training
- Homogenization
- Follow-up

Actions

- Setting up of 3 complementary data set on BAMARA
- Analysis of patient records followed in the centers over a 3-year retrospective period.
- Completion of supplemental collections for patients without a specific diagnosis
- Update of records and status of diagnosis

31646
files analyzed



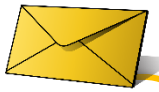
6095
In diagnostic wandering or impasse

482 patients obtained a diagnosis last year

Therapeutic Trials and Advanced/Innovative Therapies

The therapeutic trials unit has established an operating charter:

1. investigator



Submission to Filnemus by academic email address (Filnemus Web portal)

ET.Filnemus@ap-hm.fr

Web site : propose-a-therapeutic-test

2. Therapeutic Trials Unit

Evaluation of the proposal by the committee which concludes whether Filnemus supports the proposal or not

3. If favorable

The committee asks the centers that wish to participate and transmits the list to the promoter.

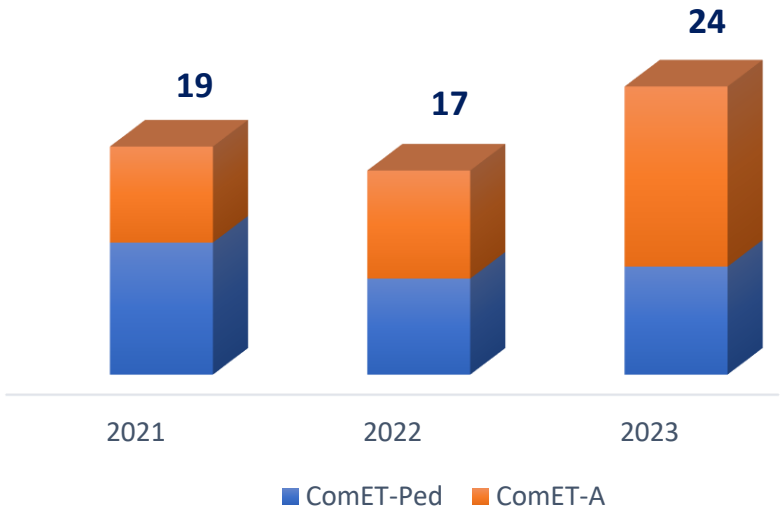
Benefits:

- A single dedicated contact, a single academic email address
- Faster and more targeted response (list of centers that can participate in this study)
- Possibility to exchange directly with the commission and to have the opinion of the greatest French experts

Since September 2020: **8 trials** have been evaluated, 6 laboratories have presented their project to the experts

Therapeutic trial commission

Therapeutic trial submission



Therapeutic trial directories accessible online

Filnemus

Filnemus Research Commission

Objective: Prioritize translational research

- One of the priorities of the Filnemus research commission is to develop translational research within the Filnemus network.

- **9 Consortia**
  - Myopathy related to Titin abnormalities
  - Calcium release myopathies
  - FSHD Myopathy
  - CMT
  - Cardiomyopathies
  - Congenital myopathies
  - Congenital Myasthenia

Conclusion: The French Network for Neuromuscular

→ **Comprehensive System**: Efficiently manages rare diseases.

→ **Coordination**: Collaborates with various centers to provide the best care, training, and information.

→ **Innovation**: Commits to pioneering therapies, preventive strategies, and supports for patients.

→ **Resilience**: Successfully navigated through significant health crises like COVID-19.

→ **Reducing Diagnostic Wandering**: Actively working to expedite diagnosis and eliminate disparities in healthcare.

→ **Neonatal Genetic Diagnosis**: Pioneered in neonatal genetic diagnosis, shaping the future of rare disease treatment.

→ **Aim**: Continuously striving for advancements and equality in healthcare access.

Filnemus