Prospective, Longitudinal study of the Natural History and functional status of patients with MyoTubular Myopathy
NatHis-MTM

Myotubular Trust Family Conference

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INSTITUTE OF MYOLOGY
CURE THROUGH INNOVATION

- **International Study**

  - ***Sponsor:*** Valerion Therapeutics – USA
  - ***Sponsor for Europe:*** Association Institut de Myologie – France
  - ***Coordinating investigators:***

EU: Dr Laurent SERVAIS
USA: Dr Carsten BONNEMANN
Canada: Dr James DOWLING

Part 1:

Study proceedings

1.1 Objectives

Primary objective

- To characterize the disease course in MTM patients using standardized evaluation

Secondary objectives

- To identify prognostic variables of the disease
- To identify the best outcome measure for further therapeutics approaches
- To assess the immune response against AAV

1.2 Methodology

Study of physiopathology

- Prospective
- Multicentric international
  - Europe: France, Belgium, Germany, UK, Switzerland, Italy
  - North America: USA and Canada
- Interventional study

Number of subjects: 60 (Europe:40)

Study duration: 36 months

Enrollment duration: 24 months

Patient's participation: 12 to 36 months

1.3 Study design

Age of the patient	Frequency of assessments
0 – 2 years old	1 visit/3 months
2 – 6 years old	1 visit/6 months
> 6 years old	First year: 1 visit/6 months After: 1 visit/year

1.5 Population

Inclusion criteria

- Any age (newborns included)
- Written consent (parent(s)/legal gardian(s) for minors)
- Myotubular myopathy from a mutation in the *MTM1* gene
- Male or symptomatic female

  Symptomatic female : MFM or NSAA < 80%.
- Willing and able to comply with all protocol requirements and procedures
- In France only: Affiliated to or a beneficiary of a social security category

  For non French patients it could be the European health insurance card

1.6 Population

Exclusion criteria

- Other disease which may significantly interfere with the assessment of the MTM and is clearly not related to the disease
- Currently enrolled in a treatment study; or treatment with an experimental therapy other than pyridostigmine
- In women : Pregnancy or breastfeeding

1.7 Specific aspects

- Visits in patient's center or at home for assessments by the physiotherapist.
- For European patients outside France: possibility to be included and to perform the first or all visits of follow-up at the Institute of Myology in Paris until opening of their centers in their own country *(Requirements: travel acceptance and possession of the European insurance credit card)*.

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- Visit duration (according to the age and the ambulant status of the patient):
  - Inclusion visit: 4 to 6 hours
  - Follow-up visits: 3 to 5,5 hours

Part 2:

Description of the PT evaluation

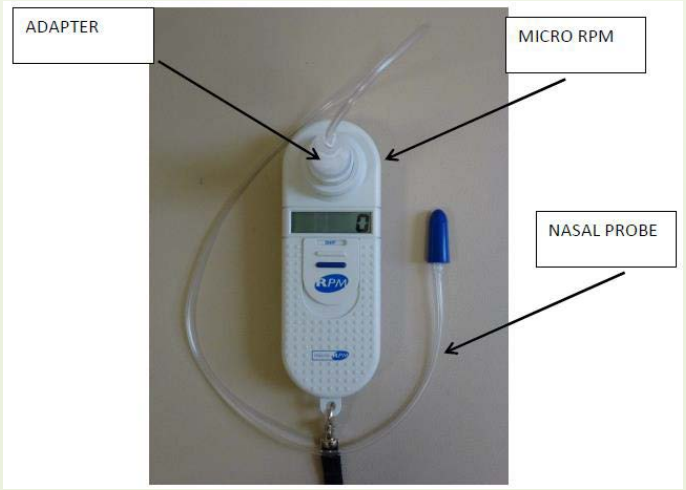
2.1 Pulmonary function tests

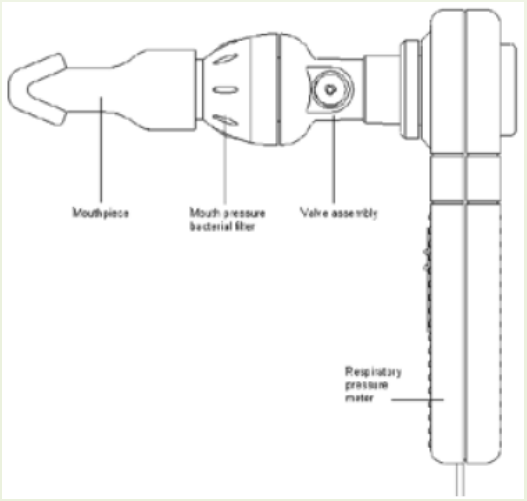
Air volume in the lungs

- Max exhaled (FVC)
- Exhaled in 1 sec (FEV1)

Peak Cough Flow

Maximum expiratory and inspiratory pressures





2.2 Strength assessments

MyoGrip:

Max. isometric grip strength through squeezing the handle

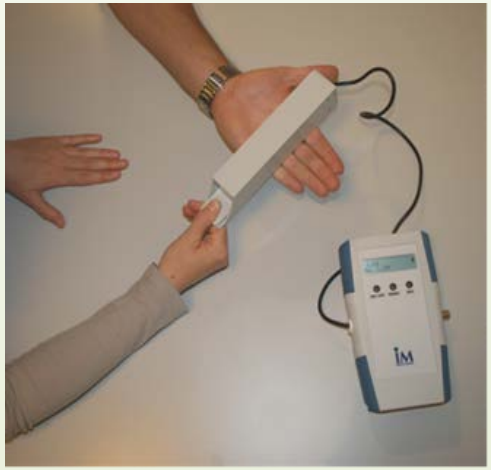
High precision

Sitting position

Standardized position,
but adaptable if necessary

MyoPinch:

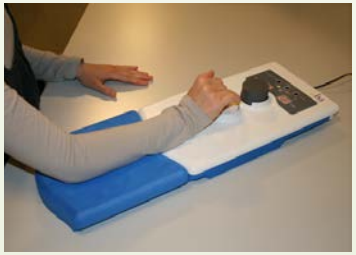
Max. isometric pinch strength



2.3 Motor function assessments

TOOL:

MOVIPLATE



TIMED TESTS:

6MWT

Time to rise from floor test

10 meter timed walk/run test

SCALES:

MHFMS

CHOP-INTEND

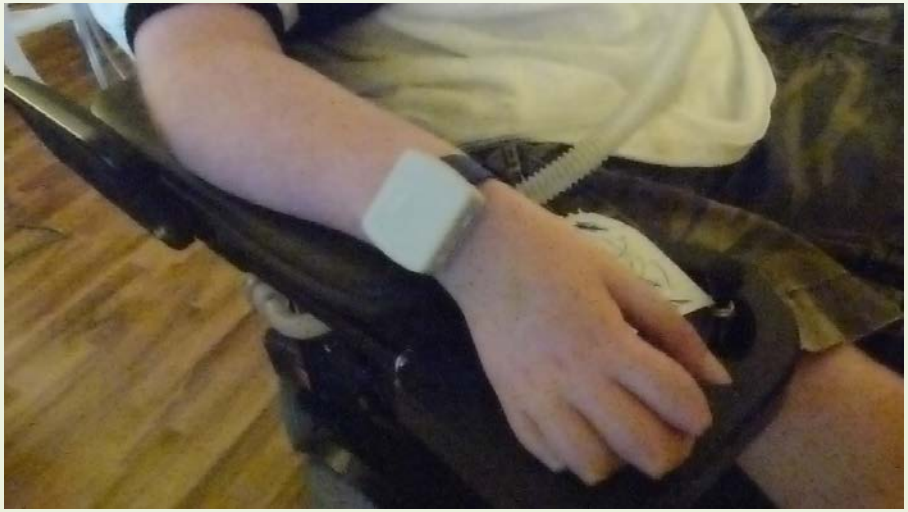
NSAA

MFM

2.4 Activity monitoring

ActiMyo

- Institute of Myology (Paris) – SYSNAV Company
- Measure the upper limb activity
- Light➔ movement not limited
- Ambulant and non-ambulant



2.5 Other informations

- Interview about the full medical history
- Questionnaire about quality of life
- Liver screening every year

NOTE: Possible adverse events between visits such as missing school, hospitalisations etc…

Part 3:

Patients

3.1 Investigational Sites

France : 1 opened CNT/ 5

- **Institut de Myologie – Paris**
- Hôpital Trousseau – Paris
- CHU – Lille
- Hôpital St Musse – Toulon
- CHU – Lyon

UK: GOSH-UCL

Germany: Essen

Italy: Roma

3.2 Selected Patients

France: 5 patients included
4 males with age 4, 11, 18, 19 years
+ 1 symptomatic femal, 38 yo

UK: forcasted: 10 patients

Germany: 7 patients already met (Hohenroda, sept 2013)

Italy: 4 (or more) italian patients + 1 swiss patient

Team

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