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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• 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

<table>
<thead>
<tr>
<th>Age of the patient</th>
<th>Frequency of assessments</th>
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<tbody>
<tr>
<td>0 – 2 years old</td>
<td>1 visit/3 months</td>
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<tr>
<td>2 – 6 years old</td>
<td>1 visit/6 months</td>
</tr>
<tr>
<td>&gt; 6 years old</td>
<td>First year: 1 visit/6 months</td>
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<td>After: 1 visit/year</td>
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Inclusion criteria

• Any age (newborns included)
• Written consent (parent(s)/legal guardian(s) for minors)
• Myotubular myopathy from a mutation in the \textit{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

\textit{For non French patients it could be the European health insurance card}
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
• 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

**MyoPinch:**
Max. isometric pinch strength

- High precision
- Sitting position
- Standardized position, but adaptable if necessary
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

2013 MTM-CNM Family Conference

www.mtm-cnm.com
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 female, 38 yo

UK: forecasted: 10 patients

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

Italy: 4 (or more) Italian patients + 1 Swiss patient
Team

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