

## TREAT-NMD Workshop Report: Outcome Measures for Non-ambulatory DMD

Paris, 17<sup>th</sup> June 2009

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On the 17<sup>th</sup> June 2009 28 participants from Europe and the US attended a TREAT-NMD workshop, also supported by the *Foundation to Eradicate Duchenne* ([www.duchennemd.org](http://www.duchennemd.org)), in Paris to discuss the selection of outcome measures for Duchenne Muscular Dystrophy (DMD) clinical trials involving non-ambulatory patients.

There are currently several groups in the process of developing non-ambulatory protocols in DMD for submission to the regulatory authorities. The aim of the workshop was to help harmonise existing efforts as well as plan for future trials. The invited workshop participants included clinicians, academics and physiotherapists as well as representatives from patient organisation and industry.

The overall aim of the workshop was to present and discuss the merits of possible outcome measure for use in DMD trials as a first step towards reaching a consensus among the neuromuscular community. Specifically the workshop aimed to;

- Address the issue of functional measures suitable for trials in non-ambulant DMD
- Consider the special case of single limb delivery where subtle changes in muscle strength will need to be detected
- Work to harmonise efforts in data collection and improve natural history

### Introduction and context

The workshop was opened by Kate Bushby and the workshop chairs Francesco Muntoni and Eugenio Mercuri.

**Elizabeth Vroom** presented the patient and parent perspective. Elizabeth noted that a 'good' outcome measure for patients is one which records a function/measure that matters (is important) to them- a point which was also made by EMEA representatives at a meeting organised by TREAT-NMD in October 2008 to discuss outcome measures for SMA trials.

**Eugenio Mercuri**, presented the lessons learnt from harmonising efforts in SMA Outcome Measures. Eugenio noted over the last 2 years the community has started to work together to decide which particular scales were the best to use to test a specific hypothesis in a specific population. The community as a whole has also learnt to work with EMEA and FDA in the initial planning stages of trials.

**Elena Mazzone** discussed the recently developed TREAT-NMD upper limb functional scale which is currently being tested by the SMA groups in Europe (as part of a project funded by SMA Europe) and will be tested by the US groups in the future- such upper limb scales may be adaptable for use in DMD. **Tina Duong** (CINRG) presented preliminary results from the CINRG/UC Davis DMD Longitudinal

Study on outcome measures in non-ambulatory DMD patients. **Elena Pegoraro** (University of Padova) presented data on the identification of a validated genetic modifier of older DMD patients and its potential importance as a co-variant in clinical studies.

### Appraisal of specific measures and harmonisation of efforts

Prior to the workshop a working group of specialised physiotherapists met to discuss the suitability of commonly discussed outcome measures for non-ambulatory DMD trials as well as issues relating to planning training programmes, coordinating training between the different groups (TREAT-NMD, CINRG, MDA) and coordinating efforts to facilitate progress. During the workshop **Michelle Eagle** (Newcastle Muscle Team) presented the physiotherapist consensus on outcome measures (including respiratory, functional scales / functional timed tests and upper limb evaluations) and fed back the plans for collaboration discussed during the session including the integration of different efforts.

The following sessions were concerned with sharing experience in different measures relevant to non-ambulant DMD and gave several researchers the opportunity to present data on measures they currently use. **Michelle Eagle** discussed data on Forced Vital Capacity (FVC). **Marion Main** presented Myometry of upper limbs in non ambulant DMD using the Cytech myometer. **Robert Pangalila** presented data on Hand function, measured with MFM and its relation to strength and range of motion in adult DMD patients. **Laurent Servais** presented preliminary data on the quantification of upper limb function in non ambulatory patients using clinical test and actimetry. **Jean-Yves Hogrel** presented information on grip strength assessment in weak patients . **Pierre Carlier** and **David Bendahan** discussed the role of assessment of MRI scans as an outcome measure for DMD. **Erik Henricson** discussed the NIH NeuroQoL project which has been validated in DMD teens / young adults. The last presentation of the day was given by **Leone Atkinson** (PTC) regarding the preparation of the PTC non-ambulatory protocol.

The round –up and discussion session was chaired by **Eugenio Mercuri** and **Francesco Muntoni** and it gave all the participants the opportunity to discuss the questions raised throughout the day. Many potential outcome measures do exist to collect data in non ambulant DMD from the perspective either of functional studies or the assessment of strength in a single limb. Some of the scales available are known to the regulatory authorities for different diseases. All require further study in the DMD population, and this comparative work is under way via collaborations between the TREAT-NMD, CINRG and MDA groups. TREAT-NMD and CINRG will establish an international working group to help move this work forward and the TREAT-NMD Registry of Outcome Measures (ROM) will be used as a tool to facilitate the collaboration.

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<b>Participant</b>	<b>Affiliation</b>	<b>Country</b>
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Emma Heslop	Newcastle University, TREAT-NMD	UK
Elena Mazzone	University La Cattolica of Rome , TREAT-NMD	ITALY
Joanne Auld	Kings College London, TREAT-NMD	UK
Michelle Eagle	Newcastle Muscle Team	UK
Elizabeth Vroom	UPPMD, Europe	NETHERLANDS
Béatrice de Montleau	AFM	FRANCE
Valerie Cwick	MDA	USA
Elena Pegoraro	Department of Neurosciences, University of Padova,	ITALY
Tina Duong	CINRG	USA
Julaine Florence	Washington University, CINRG	USA
Erik Henricson	University of California, Davis	USA
Marion Main	GOSH, London	UK
Laurent Servais	Institut de Myologie, Paris	FRANCE
Jean-Yves Hogrel	Institut de Myologie, Paris	FRANCE
Carole Berard	Hospices Civils de Lyon	FRANCE
Pierre Carlier	Institut de Myologie, Paris	FRANCE
David Bendahan	University Hospital of la Timone, Marseille	FRANCE
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