Observational Prolonged Trial In Myotonic dystrophy type 1 to Improve Quality of Life- Standards, a Target Identification Collaboration.

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**Introduction**

OPTIMISTIC is an EU funded clinical trial testing a unique cognitive behavioural therapy with the aim of increasing activity, reducing fatigue and improving quality of life in people with myotonic dystrophy type 1 (DM1).

DM1 is the most common adult muscular dystrophy worldwide estimated to affect 1 in 8,000 people in Europe. It is a complex and variable disease that effects people in many different ways. Symptoms range from muscle weakness (e.g. in the face, neck, hands and forearms), myotonia (cramping, difficulty releasing grip) to trouble swallowing, cataracts and other eye problems, heart conditions, and cognitive difficulties like tiredness and daytime sleepiness and problems with planning and thinking. There is currently no treatment to stop, slow down or prevent DM1.

This study will mainly address the cognitive difficulties faced in the population. OPTIMISTIC aims to compensate for a reduced initiative, optimise physical activity and alleviate fatigue with the ultimate objective of improving societal participation and thus quality of life. Other key objectives include identifying genetic factors that predict outcome and potential biomarkers as surrogate outcome measures that best explain the observed clinical variation.

A total of 286 patients will be recruited into this assessor blind, randomised trial. The OPTIMISTIC consortium is a collaboration of 9 partners across France, Germany, the Netherlands and United Kingdom coordinated by Baziel van Engelen at Radboud University Medical Centre, Nijmegen. The trial will take place across four clinical centres, Newcastle, Munich, Nijmegen and Paris.

**Cognitive Behavioural Therapy**

The trial intervention designed by Dr. Hans Knoop is a unique combination of cognitive behavioural therapy (CBT) and exercise, focusing on increasing the participants activity. This will be achieved through changing the thoughts and behaviour that can unintentionally maintain fatigue. This might include changing sleeping patterns or trying to increase the level of physical activity. Teaching people how to compensate for problems in taking initiative or starting an activity, e.g. by learning to schedule your activities. The study will also involve a carer or significant other where appropriate and the therapy will involve working together with significant others to discover how to best manage the impact DM1 has on daily life.

**The Trial**

- Participation in the study lasts around 17 months.
- There are five assessments visits (screening, baseline, 5 months, 10 months, 16 months).
- The intervention runs for ten months but is front-loaded, meaning the first four months can be considered the ‘active’ phase with the remaining six months in the ‘booster’ phase. In this period of ten months a patient will receive 10-14 sessions, at least five of them are face to face session.
- Participants will be randomised 1:1, with the non intervention group receiving standard care.
- Participants will be identified from the clinic lists and also using national registries.

**Inclusion Criteria**

- Genetically confirmed DM1
- Over 18 years old
- Ability to walk independently
- Ability to provide informed consent
- Score > 35 on the checklist Individualised Strength (CIS) fatigue

**Exclusion Criteria**

- Severe depression
- Participation in another clinical trial
- Unable to complete study questionnaires
- Use of psychotropic drugs (with the exception of modafinil and Ritalin)

**Outcomes**

One of the aims of OPTIMISTIC is to develop and validate clinically significant outcome measures that can be used in future trials. The primary outcome measure will be the DM1-Activ measured at the end of the 10-month intervention period. DM1-Activ is a specific outcome measure of activity and participation for patients with DM1 [Hermans 2010]. Secondary outcomes are listed below.

**Activity:**
- 6-minute walk test (6MWLT), Myotonic Dystrophy Health Index (MDHI)
- Physical activity measured with actometer.

**Fatigue and sleepiness:**
- Fatigue and Daytime Sleepiness Scale (FDSS), Checklist Individual Strength (CIS) fatigue

**Quality of life:**
- Individualised Neuromuscular Quality of Life Questionnaire (InQoL)

**Mood:**
- Beck Depression Inventory for Primary Care

**Cognitive:**
- Apathy evaluation scale (AES), Stroop test

**Future Considerations**

As the first European trial with intervention for myotonic dystrophy type 1, OPTIMISTIC marks an important step forward in the field. OPTIMISTIC is looking beyond the traditional pharmacological solutions to address the current lack of therapies that can reduce, slow down or maintain the symptoms of the condition. Working closely with the TREAT-NMD Alliance and OPTIMISTIC will engage and collaborate with the wider neuromuscular community including patient organisations and furthermore with the wider rare disease community and the efforts of IRDiRC to find 200 new therapies for rare disease by 2020.

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