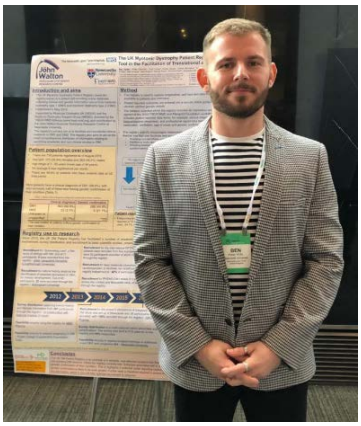
UK Myotonic Dystrophy Patient Registry Newsletter

ISSUE 7
www.dm-registry.org/uk
www.treat-nmd.org

Accelerating research and improving care in myotonic dystrophy

Remember to update your details and tell your doctors about the registry – it's important for us all to work together.

Inside this Issue:



We attended the 2019 Myotonic Annual Conference in Philadelphia on 13th September 2019. Here is the registry curator presenting the UK Myotonic Dystrophy Patient Registry and the research it has supported. The poster is available from the registry website at: https://www.dm-registry.org/uk/media/images/UK_Myotonic_Dystrophy_Patient_Registry_MDF_Conference.pdf

Welcome to the seventh newsletter of the UK Myotonic Dystrophy Patient Registry.

As of February 2020 there are 767 participants registered with the UK Myotonic Dystrophy Patient Registry. A huge thank you is in order for all of the patients, clinicians, caregivers and patient organisations who have supported and contributed to this superb achievement.

1. Please provide your genetic report where possible

Your genetic diagnosis is one of the most important pieces of information within the Registry. This is currently provided by your neuromuscular consultant if you see one. However, if you do not see a neuromuscular consultant (though we recommend you do), it is still important we have this information. If you have a copy of your genetic report this can be sent directly to the Registry curator. Alternatively you can speak to your neuromuscular consultant at your next appointment, they should be able to provide you with a copy of the report if you have been tested.

Most studies and clinical trials in myotonic dystrophy looking for participants will only include people with **genetically confirmed** myotonic dystrophy type 1 or type 2.

REMINDER - if your doctor does not appear on the registry as a selected healthcare professional then please update them about the registry at your next appointment or via email, and also tell the registry curator and they will try to contact them.

2. New studies and research updates

Activity monitoring in progressive muscle diseases – ongoing ★

This study is being run from King's College London.

The purpose of the study was to measure active and resting behaviours in people with progressive muscle weakness, and to test the quality of measurement. Participants were asked to complete various questionnaires and to wear an activity monitor at the start and end of the study. An optional part of the study was to provide participants with their own Fitbit activity monitor whilst they were monitored remotely.

The study recruited participants aged 18 years and above who had a **diagnosis of a progressive muscle disease** (such as myotonic dystrophy).

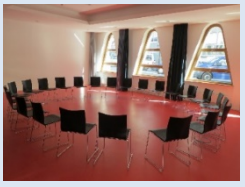
Following the promotion of this study through the registry, 108 participants expressed interest in taking part, however, only 5 participants were included in the study. This was due to limited study capacity and high interest across all conditions. Results will be shared once the study has concluded.

Patient and caregiver dysphagia advisory group – ongoing ★

This study is being run from University College London Hospitals Foundation Trust.

The first stage of the study was to build a patient and public involvement (PPI) group who have experience of dysphagia (swallowing difficulties). The group shared their experience of dysphagia (as a patient or caregiver) which has helped develop questions for a survey that would be sent out through the UK Myotonic Dystrophy Registry in the near future.

As of September 2019, there were 25 people with myotonic dystrophy type 1 interested in taking part with 21 of those coming from the registry. The group have met twice (in Nov 2019 and Jan 2020 and have been liaising via email intermittently). A survey is currently in development looking at swallowing problems in neuromuscular diseases, which will hopefully be circulated through the registry soon.



END-DM1 natural history study

A new research study, entitled, "Establishing Biomarkers and Clinical Endpoints in Myotonic Dystrophy Type-1 **(END-DM1)",** is being conducted at 9 sites around the U.S, as well as potential sites in Europe (including the UK).

The study is designed to help drug developers successfully design clinical trials and understand how to assess the effectiveness of potential therapies. This will be done by measuring whether myotonic dystrophy is getting better or worse, and determine how it changes over time.

This study will enroll 500 people, ages 18-70, with **myotonic dystrophy type 1.**

For further information on the study requirements please visit:
https://clinicaltrials.gov/ct2/show/NCT03981575

Natural history study collects health information in order to understand how the medical condition or disease develops and how to treat it.

Genetic factors that determine disease severity in myotonic dystrophy type 1 – results from the OPTIMISTIC cohort

Dr. Sarah Cumming and Professor Darren Monckton, together with the rest of researchers of the OPTIMISTIC trial, recently published a scientific paper that identifies genetic factors that impact on the severity of myotonic dystrophy, and that play a role on how early patients might start experiencing symptoms - https://doi.org/10.1212/WNL.0000000000008056

Background

Myotonic dystrophy type 1 (DM1) is an inherited genetic disorder caused by a mutation in which a triplet of letters in the DNA, CTG, appear with more copies than they should. In the general population there are up to about **40 copies** of the CTG repeat. However, in DM1 patients this triplet has **increased in size to more than 50**, and can be as many as 1,000 in some people. The more times these CTG repeats appear consecutively, **the more severe the disease** will present and the earlier that symptoms will appear. Notably, the number of repeats nearly always increases when passed on from one generation to the next, mediating the decrease in age at onset often observed in DM1 families. The number of CTG repeats also increases during the lifetime of the individual, which in addition to hastening disease onset, can complicate our ability to interpret the results of genetic testing.

Method and results

Researchers at the University of Glasgow analysed blood DNA samples provided by 255 participants of the international **OPTIMISTIC study** (including patients from the Netherlands, France, Germany and UK) The researchers determined the average number of CTG repeats that patients had during the start of the trial, and estimated how many CTG repeats were inherited from their parents when conceived.

The results show that the number of repeats inherited:

- Determines the age at which symptoms first appear in a patient.
- Predicts clinical manifestations of the disease such as muscle function and walking performance, and the capability of patients to perform daily life tasks.
- Seems to delay the appearance of the first symptom by almost a decade in a small number of patients (about 8%) who have variant interruptions. This is also associated with an overall lower disease severity and is consistent with the observation that the presence of the variant repeat interruptions slows down the rate at which the CTG repeat grows during the lifetime of an

Implications for clinical trials and new therapies

"These results confirm the importance of carefully counting the number of CTG repeats as part of clinical trials in DM1 and increase prospects for detecting the effects of new treatments. In addition, our finding that the increasing number of CTG repeats contributes toward both the age at onset, and severity of the many of the progressive symptoms, reinforces the idea that stopping the repeat getting bigger during the lifetime of the patient would be therapeutically beneficial."- Professor Darren Monckton

REMINDER - If the registry is used to promote or assist with the recruitment for a clinical trial or research study, all potential eligible patients will be contacted by the registry curator via email.

3. Treatments in development and how to get involved in clinical studies

Tideglusib is an oral treatment developed by AMO Pharma. It is designed to reverse cognitive and behavioural deficits by stopping an enzyme that is overly expressed. Tideglusib appeared to provide some benefit to some adolescents and adults with congenital and juvenile-onset myotonic dystrophy, after 12 weeks of treatment in a previous study.

To confirm these preliminary findings, AMO Pharma is initiating a phase II/III clinical trial in the USA, Canada and the UK (Newcastle), in 6-16 year old children with **congenital myotonic dystrophy**. The trial is expected to begin in April 2020. See: https://www.clinicaltrialsregister.eu/ctr-search/trial/2016-004623-23/GB or https://clinicaltrials.gov/ct2/show/NCT03692312.

ERX-963 is a treatment developed by Expansion Therapeutics that is designed to reduce excessive daytime sleepiness and improve cognitive function in **DM1.**

Expansion Therapeutics have a current phase I clinical trial in the USA that is expected to end in Feb 2020. See: https://clinicaltrials.gov/ct2/show/NCT03959189.

Pre-clinical research

There is also a wide range of pre-clinical research occurring in myotonic dystrophy which includes:

5 gene therapies

For further information on potential therapies in development please visit: **https://www.dm-registry.org/uk/media/images/Myotonic_Dystrophy_Drug_Development_Pipeline.pdf**

Pre-clinical research is important laboratory work done using cell models and animal models to firstly identify a new drug and to then test it to see if it is safe and effective before being tested in humans. This can take between 1-5 years.

Gene therapy involves replacing a faulty gene or adding a new gene to treat or stop a disease.

How do I take part in a clinical trial?

You can search the **Be Part of Research** site to find trials relevant to you, and you can contact researchers yourself to potentially get involved - https://bepartofresearch.nihr.ac.uk/. Using this site enables you to search for trials in the UK near to where you live, and based on your condition. Alternatively you can ask your doctor or a patient organisation about any ongoing clinical trials that you may be eligible for.

Clinical trials often involve comparing the effects of one treatment with another and can involve patients, healthy people, or both. To learn more about clinical trials and the process of getting involved in research see: https://www.nhs.uk/conditions/clinical-trials/

4. Previous and upcoming events and new initiatives

In December the registry was presented at the **6th TREAT-NMD International Conference** in Leiden, where there were many academics, patients, carers, patient advocacy organisations, clinical specialists and industry. Following directly on from this meeting, the registry was discussed at the **TREAT-NMD Global Database Oversight Committee (TGDOC)** meeting with registry curators across the globe, to discuss best practice and future plans.

Upcoming events

- **Myotonic Dystrophy Support Group (MDSG) Regional Meeting -** this will be held at the Hawker Centre, YMCA Hawker, Lower Ham Road, Kingston KT2 5BH on 4th April between 2pm and to 5pm. Please telephone Penni Cotton on 07891 412461 or email penni.cotton@gmail.com for more details. There will be refreshments available and there will be a speaker on orthotics.
- **MDSG 31st Conference and Annual General Meeting** – this will be held at the Radisson Blu Hotel, Herald Way, East Midlands Airport, DE74 2TZ on 19th and 20th June 2020. For further information see: contact@mdsguk.org
- **2020 Myotonic Annual Conference** – this will be held at Paradise Point in San Diego, California on 11th and 12th September 2020. For more information please visit: https://www.myotonic.org/2020-myotonic-annual-conference

New initiatives

The public layer of **Share4Rare** includes curated medical content, written by medical experts and reviewed and approved by patients and carers living with the disease. Validated users can also access a secure area where you can share questions but also help others by answering their questions, and be matched with other users who have a similar diagnosis and/or symptoms.

The platform is currently recruiting adult neuromuscular patients and caregivers as they will be developing quality of life/burden of illness questionnaires aimed at the neuromuscular community. Click on https://www.share4rare.org/registration/s4r to register for Share4Rare to become part of the community and to participate in the upcoming pilot study.

Thank you all - there has been a great response from the registry so far! If you have any questions please contact Avril Palmeri at avril.palmeri@ncl.ac.uk

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Thank you for being a part of the UK Myotonic Dystrophy Patient Registry. **Please remember to log in to the registry to update your data if you have not already done so within the past 12 months.**

If you have any questions, feedback/suggestions or you would like to share your story, please contact below. Also please feel free to promote the registry in any support groups you may be a member of.

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