UK Myotonic Dystrophy Patient Registry Newsletter

Spring 2017

www.dm-registry.org/uk

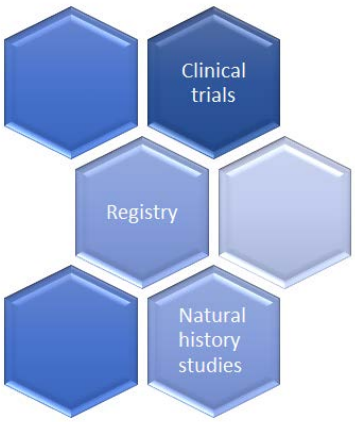
The registry is only as useful as the information it contains
Remember to update your details!

There are now over 650 people with DM1 involved in the registry! We are pleased to see the registry is still growing and would like to thank you all for being involved. The registry has proved useful for a number of different research studies and as research into myotonic dystrophy in the UK continues to grow we would like to use the newsletter to explain more about clinical research, what that means, and how you can be involved.

What is Clinical research?

Clinical research is a branch of science that involves people, but it can take a number of different forms. In this newsletter we want to introduce you to the different types of study.

Different types of clinical reseach



There are two main types of clinical research studies that we will be discussing here.

N**atural history studies** are a type of clinical research study that involve observing the normal progression of a disease and measuring certain traits and functions. They typically involve a variety of tests repeated over a series of months or years. A natural history study does not involve any new treatments or therapies.

Clinical trials typically involve the testing of a new treatment or therapy in people. This includes new drugs. These studies are used to determine how safe and how effective new medications and treatments might be. They are also referred to as interventional studies.

Clinical research in myotonic dystrophy going is increasing compared to previous years. A number of natural history studies are being carried out in the UK and pharmaceutical companies are in the early stages of clinical trials. These different studies are described late in this newsletter.

All clinical research studies are carried out in carefully controlled conditions adhering to strict rules and regulations. It can involve lots of new words and phrases. You can obtain more information online at www.clinicaltrials.gov. You can discuss anything you read here with your doctor who might be able to answer any questions.

Natural History Studies:

One thing about myotonic dystrophy that makes it hard for doctors, researchers and scientists to understand is how it affects people differently. This will make it hard to know if a drug is working or not. Natural history studies follow large numbers of people with myotonic dystrophy to measure what is the same and what is different in people. This will help identify patterns or groups of people who are affected in the same way.

Natural history studies also look to see what changes over time and how long it takes, this is important if a drug is developed that slows down the progression of the disease.

A natural history study is like the control group of a clinical trial, it shows what is “normal” for people with myotonic dystrophy. If something is changed, for better or worse, by a new treatment it is important to be able to identify that.

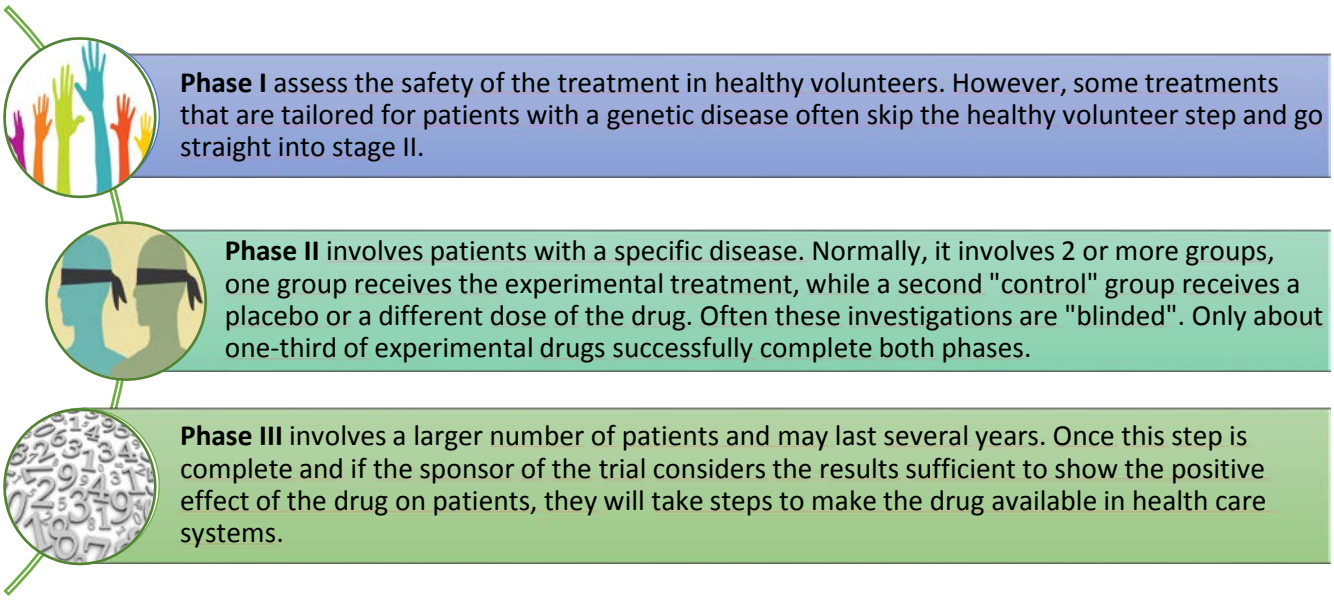
Natural history studies often include lots of different tests and measurements, these are known as outcome measures. Natural history studies are often used so that we can test to see which outcome measures work best. More about outcome measures is described later in this newsletter.

Clinical Trials

Clinical trials are designed to test new treatments and therapies both to see if they are safe and if they work as expected. It is important to understand, that just because a new treatment is in a clinical trial it does not mean that it will be safe or even effective. A clinical trial is a test to find that out.

What are the different phases of clinical trials?

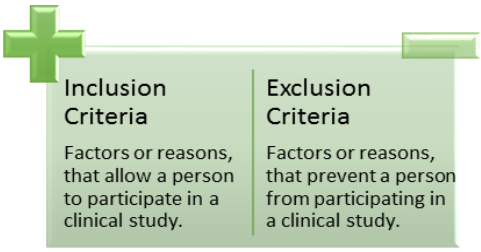
Before a new treatment or therapy can be approved for general use it must go through a number of trials. These different trials are called phases. There are usually three phases (phase I, phase II, phase III) and each phase builds on the results of the previous step. Although positive results in an early phase may be encouraging, it does not guarantee that a new treatment or therapy works. As a treatment or therapy moves through these phases they require more people to be involved and the design can change depending on the research question. Below we describe the different phases in more detail.



The role of Pharmaceutical Companies in Clinical trials.

Normally a new treatment or therapy is developed by a pharmaceutical company. These companies usually provide the funding for clinical trials. They are in charge of the design of the trial and they decide if a trial is successful enough to move to the next phase. Pharmaceutical companies normally work closely with researchers and doctors to ensure the greatest chance of success.

Who can take part in clinical trials?



It is not possible for everyone to take part in a clinical trial. There are strict rules about who can and cannot take part, these are called ***inclusion and exclusion criteria***. These criteria are often needed to ensure that the people taking part are put at as little risk as possible. These criteria are also put in place to make sure it will be possible to see if the drug is working. For example if it is proposed that a drug reduces pain, it would not be possible to test this in a group of people who do not experience pain. These criteria are often very detailed and complex, if you have questions about the criteria of a specific trial it is always best to discuss them with your doctor in the first instance.

The first time you visit any clinical trial site you will take part in a screening visit. These visits are an opportunity for the staff involved in the trial to check if you meet the criteria.

How are trials designed?

Every clinical trial is designed slightly differently this is because they are all answering slightly different questions. The design of a study can depend on lots of different factors such as how many patients might be available to take part, or the type of treatment or therapy being developed (e.g. a tablet or an injection)

However, there are some common terms used when describing trials and some of these are listed at the side of this page.

Placebo

A Placebo is a "dummy" version of a drug. They are made to have the same appearance as the treatment being tested, however, do **not** contain an active substance that will affect health. These are administered to what is called the control group in a trial. This is sometimes necessary so that researchers have a group of patients having exactly the same experience as those taking the drug to see if there is any difference. However, not all studies use a placebo. When placebo is not applicable, usual care will be the method of control.

Randomised study

When a study involves a placebo it is often related to a randomised controlled trial. This means that it is completely by chance if the person involved receives the active treatment or the placebo. The researchers involved have no control over which group their patients/participants are in. It is normally decided by a computer and there is a 50/50 chance you will receive the placebo. Not all studies using a placebo are designed in the same way.

Blinded study

When a placebo is involved in a study it is important that the research team do not know who is receiving the active drug and who is receiving the placebo. This prevents the researchers from acting differently around the participant, and stops them from making different decisions during assessments. This means that a study is blinded.

Outcome Measures

An **outcome measure** is a test that is used to determine how well a new treatment or therapy is working. This is used at the start of a study and then at every visit so that change can be measured. In diseases such as myotonic dystrophy outcome measures are often functional and involve a physiotherapist. However, they can also be questionnaires or the results of blood tests and scans.

Biomarkers

Biomarkers are types of outcome measures that do not test functional change. They are changes in the body that can be measured; this could be a certain molecule in your blood, or the amount of muscle that is seen on scan of your leg.

How do we know if a clinical trial is successful?

A crucial thing about a clinical trial is to be able to accurately measure if a drug or therapy is working or not. Not all drugs will reverse all symptoms so sometimes it might be a subtle change. When a clinical trial is being designed, you must choose one aspect of the disease to be your "primary outcome measure". This is the thing you are looking at for change, if this aspect of the disease improves then your drug works.

It is important that the outcome is easy to measure and sensitive to change. Some examples of outcome measures that can be included in trials are:

- Time to walk 10 meters
- How many times you can sit and stand (30 sec.)
- A measure of pain
- A breathing test

If the outcome measure that is chosen doesn't show change it will take longer to determine if a trial is successful, it could even mean that research into that drug will stop.

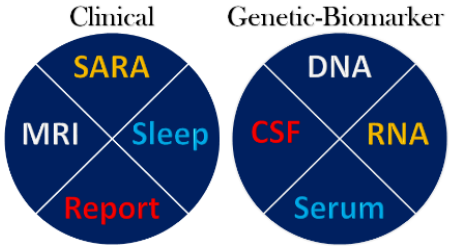
As you can see, there are many different steps involved in clinical research.

There is lots of work being carried out to move things forward as fast as possible. In the rest of this newsletter we will discuss some of the clinical research studies that are ongoing in the UK and around the world at the moment.

Natural History Studies in the UK

PHENO-DM1 (A Natural History Study)

PHENODM1 is an academic-led Natural History Study taking place in Newcastle and London. It has been funded by the National Institute for Health Research (NIHR) and the Wyck Foundation. This study is important for understanding as much as possible about myotonic dystrophy type 1 and how it affects people in different ways.



It includes clinical and functional outcomes such as muscle MRI, sleep studies and patient reported outcomes (questionnaires) that will assess muscle wasting, sleep disorders, fatigue levels and quality of life of patients. Genetic and molecular biomarker analysis will be carried out using DNA, RNA, serum and CSF samples obtained from all patients at baseline and follow-up visits. This study will complement the work of other groups currently looking at myotonic dystrophy type 1 using the same outcomes ensuring that direct comparisons can be made which will be essential for future drug development.

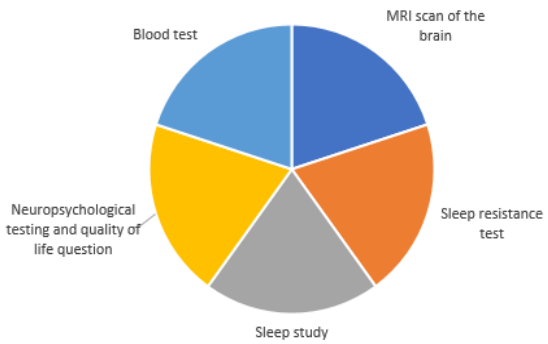
The study is now **closed to recruitment**, this means no-one new can take part. A total of 213 adults with myotonic dystrophy type 1 have been recruited (some recruited through the registry). Preliminary results will be available later this year with final results expected at the end of 2018 after the study has been completed. If you would like to know more about this study, contact Dr. Nikoletta Nikolenko on 07870 517410 or email: Nikoletta.nikolenko@newcastle.ac.uk or visit clinicaltrials.gov

DM1-Neuro

DM1-Neuro is a natural history study specifically looking at the brain in myotonic dystrophy is being carried out in Scotland, led by Dr Mark Hamilton from the University of Glasgow who received a Muscular Dystrophy UK Clinical Research and Training Fellowship.

The aim of the study is to understand why some important symptoms of myotonic dystrophy type 1, such as excessive sleepiness, sleep disturbance and impairment of thinking, vary so considerably from one person to the other. The researchers will look at how changes in the DNA and on MRI scans of the brain relate to the severity of symptoms of people with myotonic dystrophy.

The study aims to recruit 40 participants in the West of Scotland who have the adult-onset form of myotonic dystrophy type 1. While it is not testing any treatments, the study will improve our understanding of how genetic factors influence the severity of brain-related symptoms of the condition, as well as identifying the most effective ways to measure these symptoms. Both of these are important steps to improve readiness for trials of new treatments for myotonic dystrophy.



Furthermore, by contributing to better understanding of how the condition affects the brain, the study may help identify how new treatments for symptoms, such as excessive sleepiness could work, as well as determining whether people could be offered more specific information about how myotonic dystrophy is likely to affect them in the future. Preliminary results are expected by the end of 2017.

If you wish to know more about this research study, you may contact the West of Scotland Clinical Genetics Service on 0141 354 9201

There is also more information on Muscular Dystrophy Campaign Website (www.musculardystrophyuk.org)

Nottingham pilot longitudinal study

Dr Sedehizadeh, supported by Professor David Brook, Dr Paul Maddison and Dr Margaret Phillips, has been following a group of more 60 people with myotonic dystrophy type 1 (22 recruited through the registry!) measuring a range of different functions including muscle strength and walking ability to see how these have changed over time.

Work of Prof Brook's group, that involved screening thousands of compounds, identified 12, which are promising to reduce the problems caused at the molecular level in myotonic dystrophy. The scientists are now focusing on two of these compounds to further understand how they work.

The first results have been published recently. We have written a summary of this study below, if you would like to read the full scientific publication you can find it here, if you are interested in more detail, please follow this link.

Summary of Nottingham Pilot Study "Body composition and clinical outcome measures in patients with myotonic dystrophy type"

This study used a number of different assessments including a DEXA (a scanning device which measures body mass), the 6-minute walk test and measures of muscle strength in different areas. The study showed a significant decline in grip strength and finger flexion over 18 months and found the muscles involved in this tend to be affected early on in the course of the disease. The study also showed over 18 months that the fat-free body mass reduced, while fat mass increased in DM1 patients. This suggests DEXA could be a useful outcome measure for use in clinical trials.
These results should be considered when designing future therapeutic clinical trial design.

Clinical trials in myotonic dystrophy type 1

Phase II trial of Tideglusib (A clinical trial sponsored by a pharmaceutical company)

A pharmaceutical company called AMO Pharma is carrying out a phase II clinical trial testing a new drug called Tideglusib. This is the first and only clinical trial involving a company and a new drug to take place in Europe for myotonic dystrophy type 1. This a single centre trial with the only trial site being the John Walton Muscular Dystrophy Research Centre, at Newcastle University. Professor Hanns Lochmuller is the principal investigator. This means he is responsible for everything that happens in the trial.

What is Tideglusib?

In people with myotonic dystrophy type 1 too much of a molecule called GSK3β is produced. This molecule is involved in causing some of the symptoms seen in myotonic dystrophy type1. Tideglusib stops the production of this molecule. Researchers think that reducing GSK3β may help to reduce some of the symptoms experienced.

This trial has very strict inclusion criteria and not all people with myotonic dystrophy type 1 can take part in this study. Tideglusib is being tested only on people who are currently between 16 and 45 years old and who experienced their first symptoms before the age of 12. The primary purpose of this study is to test if Tideglusib is safe in people with myotonic dystrophy type 1. This trial is still open to recruitment. If you are interested in taking part, please get in touch with one of the doctors listed below:

Dr. Tiago Gomes on +44 191 241 8989 or email: Tiago.Gomes@ncl.ac.uk
Dr. Nikoletta Nikolenko on 07870 517410 or email: Nikoletta.nikolenko@newcastle.ac.uk
There is more information about this trial on the AMO Pharma website www.amo-pharma.com and clinicaltrials.gov.

IONIS-DMPK$_{RX}$

(A clinical trial sponsored by a pharmaceutical company)

The registry has previously reported on the clinical trial of IONIS-DMPK$_{RX}$ taking place in the USA. This was the first drug trial to take place in myotonic dystrophy and was using an approach known as RNA anti-sense (you can read more about that here). IONIS the pharmaceutical company who were running the trial have recently released a statement to say they will not be continuing to test this drug.

While a lot has been learned about carrying out trials in myotonic dystrophy from this experience it is disappointing news. The drug itself was safe and at the molecular level some positive outcomes were seen however it was not possible for enough of the drug to reach the muscles of patients with DM1 for it be effective. IONIS will continue to work in the area of myotonic dystrophy and are looking at how to make a better drug.

The Myotonic Dystrophy Foundation has up to date information about this trial that you can read here: http://www.myotonic.org

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Thank you for reading this newsletter and being part of the UK Myotonic Dystrophy Patient Registry. If you have any questions then please get in touch, registries@ncl.ac.uk.

Our next newsletter, we will focus on basic or pre-clinical research. This is research that is carried out in laboratories, if there is anything else you would like to see in the newsletter please get in touch. The registry is made possible through grants from the Myotonic Dystrophy Support Group and Muscular Dystrophy UK. Both charities provide help and support to people living with myotonic dysrophy.

Muscular Dystrophy UK
Fighting muscle-wasting conditions

Myotonic Dystrophy
SUPPORT GROUP

TREAT-NMD
Neuromuscular Network