TREAT-NMD
Neuromuscular Network

TREAT-NMD
Serving the neuromuscular community
Introduction

Neuromuscular disease—a rare condition

A rare disease or condition is defined as a disease that affects less than 1 in 2,000 people. Neuromuscular diseases (NMD) are among these rare diseases. They are complex and progressive, often affecting multiple body systems. NMD are often the result of genetic mistakes (or mutations) that affect muscle stability, the ability of muscle to regenerate or interrupt the communication between nerves and muscles. The rarity and diversity of NMD contributes to some of the challenges faced both for providing good quality healthcare and for conducting ‘translational’ research in the neuromuscular field.
Overview of patient involvement in treatment development

Patients are important partners in the translational research process and the diagram below illustrates how valuable patient involvement is.

- **Research Priorities**
  - Setting research agenda for treatment development
  - Donating tissue samples to BioBanks

- **Research Design & Planning**
  - Patient registries (enrolment)

- **Research Conduct**
  - Participating in clinical trials
  - Patient reported outcomes

- **Communication & Regulatory Affairs**
  - Contributing to targeted communication to patients
  - Health technology assessment
  - Regulatory affairs (e.g. involved in the preparation of guidelines & policies)

**Patients have a unique perspective:**

Patients are individual experts on their condition and can contribute their real-life experience to help make health related decisions. By taking an active role, patients can help to identify gaps in research priorities, participate in clinical trials, become members of committees and advisory boards, as well as help contribute to the preparation of health guidelines. Patients therefore play a key role in all areas of health-related research, which helps to support new treatment development and healthcare provisions.

Translational Research

"Turning research discoveries into therapeutic treatments that benefit patients"

So what is translational research and why is it important?

Translational research aims to develop discoveries in the laboratory towards drugs or interventions that are available to patients. This process is sometimes referred to as "Bench to Bedside". Every step of this process is important. The early phases answer questions about the disease, what causes it and evaluates whether potential therapies in theory are working in disease models. The ultimate aim is to develop drugs and interventions that will improve the quality of life of patients.

Translational research involves many different partners including scientists who make discoveries and pharmaceutical companies who help contribute to research findings and fund the development of new treatments. Patient organisations help to speed up the drug development process by supporting patient involvement in research and by providing funding to promote scientific advancements. Patients also play an important role in translational research in lots of different ways, including sharing their experience of their condition and by taking part in clinical trials to help test potential treatments.

Knowledge gained from research in a laboratory is used to develop new treatments that directly benefits patients.

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* TREAT-NMD advisory committee for therapeutics (TACT)
TREAT-NMD tools and resources

There are specific tools that are needed for therapy development and TREAT-NMD has developed a number of essential tools that continue to help accelerate translation research. These include ‘Outcome Measures’ which are the tests that help clinicians decide whether a treatment being tested in a clinical trial is having any effect. Another important tool that TREAT-NMD has helped to establish are ‘Biobanks’ which are collections of human tissue samples donated by patients. TREAT-NMD has improved the availability and the exchange of patient samples among scientists across Europe to help accelerate research studies and the development of new treatments for neuromuscular conditions.

TREAT-NMD partnership support translational researchs

Since 2007, TREAT-NMD has been central in bringing together the right experts, patients, patient organisations, scientists, healthcare professionals and pharmaceutical companies. By uniting these experts within the neuromuscular community, TREAT-NMD has been able to support new promising findings in research in animal and cell models that raise the potential for new therapies in the future. TREAT-NMD has successfully developed a number of key resources (outlined in the table below) that benefit patients, researchers, clinicians and pharmaceutical companies.
What are clinical trials?
Clinical trials are research studies that involve patients or healthy people and are designed to test the safety and effectiveness of a treatment (e.g. new drug) in a controlled setting. The data obtained in clinical trials is extremely valuable as regulatory agencies use the results of trials to decide whether to approve drugs and make them available for doctors to prescribe them to their patients. Clinical trials also help to improve the care and quality of life of patients who are ill by ensuring they receive the best standard of care. Clinical trials are divided into 4 phases (I, II, III, IV) and each phase builds on the results of the previous stage (see diagram on adjacent page). Although positive results in an early phase clinical trial may be encouraging, it is never a guarantee that the drug will work. The next step (late phase) is always more complicated due to complex trial designs and the larger number of participants involved.

While it is possible for academic groups to coordinate (or ‘sponsor’) clinical trials, due to the logistics, administration and money involved, clinical trials are usually coordinated by pharmaceutical companies. Especially for rare diseases, expert healthcare professionals are often involved in advising on trial design and will treat the patients participating in the trial.

Early phase of clinical trials
The early phases of clinical trials are designed to discover how the drug is taken up and processed by the human body and if the treatment is safe. This part of the trial is usually carried out in healthy volunteers and then in patients. However, some personalized therapy treatments that are tailored for patients with a genetic disease (e.g. exon skipping and gene therapy) often skip the healthy volunteer step and go straight into patients.

Late phase of clinical trials
The later phases of clinical trials involve testing the treatment in a larger number of patients, in order to find out how well the treatment works, how long the effects last and identify any potential side effects. These phases also help to determine the effective/safe dose of the treatment. If the sponsor of the trial considers the results sufficiently promising, they will submit all the data to the regulators (e.g. EMA or FDA) to request ‘marketing authorisation’ for their treatment. Once the regulators evaluate all the evidence, they assess whether the ratio of the benefit and the risks of the proposed treatment is favourably balanced. When it is, the therapy will receive marketing authorisation (i.e. it will be approved).

What is post marketing surveillance?
Post marketing surveillance (PMS) is required by the regulators once a drug treatment is approved, and is sometimes referred to as Phase IV. The aim of PMS is to evaluate the safety and effectiveness of a drug when it is in actual use in patients outside of the strict clinical trial criteria (‘real world use’). PMS data is collected on every patient receiving the drug, or at least on an agreed number of these patients, and is usually part of a long-term data collection process that can run for a period of about 5-15 years. It is important that the data and information collected on the safety and effectiveness of a drug is stored in a certified, regulatory compliant PMS database. This data must be accurately collected, kept confidential and is anonymised for each patient. The data stored in the PMS database is only accessible to health professionals, the trial sponsor and the regulators to help them reliably measure the health and quality of life of patients.
Case Study: Global patient registry and care and trial sites registry enquiry

Pharmaceutical companies may request information from the TREAT-NMD patient registries and care and trial sites registry (CTSR), as part of their 'Clinical Trial Feasibility' assessment. Clinical trial feasibility is the process of evaluating the possibility of conducting a particular clinical trial and involves identifying the potential barriers and delays that could have a negative impact on a trial. Examples of the information requested by a pharmaceutical company include:

From the global patient registry:
- Numbers of patients with specific mutations
- Numbers of patients in categories such as patients by age range and ambulation status
- Total numbers of patients per country meeting specific inclusion criteria from over 40 countries worldwide

From the CTSR:
- Information on trial sites including equipment and staffing, muscle biopsy experience, clinical trial experience
- Details of site diagnostic capabilities e.g. availability of specific genetic tests

This information can dramatically speed up trial planning and remove the barriers to getting a trial established to test a potential drug. At the recruitment stage, eligible patients can subsequently be contacted through their national registries in parallel with clinical trial site-based recruitment efforts.

What is a patient registry?
A patient registry collects information related to people with a specific condition and they play an important role in clinical research. For patients, the registries are a valuable way of keeping up to date with news related to their condition and provide an important connection to the research community.

Patient registries

Why do we need patient registries?
Patient registries allow people who may be eligible for clinical trials to be contacted quickly and easily. These registries also allow research and questionnaires on care and disease progression (also called natural history) to be conducted. This is especially important for rare neuromuscular conditions, since without a patient registry, finding enough patients for a trial could take years, and this can delay the testing of potential therapies.

Why should I register?
- Registering may open up opportunities to take part in clinical trials and other studies including natural history studies
- Registries aim to speed up the development of new therapies for neuromuscular conditions
- Registries help to keep people up to date with information relevant to their condition through newsletters that include information on the latest research developments and care guidelines
- Registries help specialists gain more knowledge about the number of people affected by the condition and how the condition progresses - information that is vital for planning the best medical care

Who enters and holds your data?
Patient registries are managed by curators who can be volunteers (e.g. patient families), charities or healthcare professionals. The information entered into a registry is provided by either the patient themselves or the professionals involved in their care (or both), after the patient has given consent for them to do so. Registries are governed by an oversight committee that includes doctors, scientists and patient organisations. It is their responsibility to monitor the registry appropriately and to review any requests for data, for example from a company planning a clinical trial.

How to join a registry?
Patient registries have been set-up for various neuromuscular conditions and a list of registries by disease can be found at treat-nmd.eu/nationalregistries
TREAT-NMD: Improving patient care

At the heart of TREAT-NMD is a commitment to bringing patient benefit through partnerships. TREAT-NMD unites clinical and scientific leaders in the community, patient advocacy groups and pharmaceutical companies to help support and promote the development of resources for new therapies and improvements to patient care. TREAT-NMD also interacts with regulators (including the EMA) through organising stakeholder meetings.

1) Addressing all inherited neuromuscular diseases:
TREAT-NMD has built many strong global partnerships across the neuromuscular community. Thousands of patients, researchers, clinicians and organisations worldwide have been able to use the resources (e.g. patient registries, training and education) developed by TREAT-NMD, which are recognised to be of benefit to all inherited neuromuscular conditions.

2) Supporting ‘clinical trial readiness’:
TREAT-NMD provides expertise and guidance to researchers, pharmaceutical companies and the wider neuromuscular community to help support ‘clinical trial readiness’ and help accelerate development of new therapies for unmet medical needs within the neuromuscular community. TREAT-NMD has a number of valuable resources used to help support therapy development at all stages, including patient registries.

Case Study: TREAT-NMD partnering with EURORDIS on ERNs

The European Organisation for Rare Diseases (EURORDIS) is dedicated to empowering people living with rare diseases and to improving their quality of life. EURORDIS (a non-governmental alliance), in partnership with over 700 rare disease patient organisations in 63 countries, cover over 4,000 rare diseases. It is therefore the voice of tens of millions of patients within rare disease communities throughout Europe.

Most NMD (neuromuscular diseases) need multidisciplinary care. Furthermore, their rarity and diversity raise challenges both for healthcare provision and for research. The creation of European Reference Networks (ERNs) involving the participation of patients, patient advocacy groups, researchers and healthcare professionals is an initiative which aims to effectively address these challenges. ERNs will be built upon rare disease groupings (e.g. EURO-NMD) and their purpose is to improve diagnosis, care and treatment for people with NMD.

EURORDIS is developing a European Patient Advocacy Group (ePAG) for each ERN disease grouping. ePAGs will bring together elected patient representatives and affiliated organisations who will ensure that the patient voice is heard throughout the ERN development process. TREAT-NMD used its communication channels to support EURORDIS to recruit members of the neuromuscular ePAG.

TREAT-NMD strong partnership with EURORDIS, is an excellent example of what can be achieved with networking and exchange of knowledge. TREAT-NMD’s high level of networking experience in the NMD field has already helped to attract more experts, patients and patient advocacy organisations to join efforts on NMD. We now hope to build upon the work that has already been established in the field through the EURO-NMD to advance both care and research for people with NMD.
Standard of care for patients with neuromuscular conditions

The relative rarity of individual NMD means that until recently there has not been any agreement among doctors about how best to care for patients, and care standards differ not only from country to country but also even within individual countries. Not only does this impact on quality of life, it also makes clinical trials of promising new treatments much harder to carry out, because it is impossible to compare results from different centres if patients are cared for in different ways.

TREAT-NMD has played an important role in producing agreed care guidelines to make best-practice care more widespread across the world. Guidelines currently exist for CMD, DMD and SMA, and are in development for other conditions. As well as the academic consensus documents, ‘family friendly’ guides for CMD, DMD and SMA have been created, written in a style that is more accessible to those without a medical background. TREAT-NMD believes it is crucial to have standards of care available in patients’ and clinicians’ native languages, and is working towards providing standards of care in several different languages. Translations are available on the TREAT-NMD website (See treat-nmd.eu/SOC).

How to get involved

There are many ways you can keep up to date with news from the neuromuscular community and get involved to influence and improve potential therapies and healthcare services:

- Become a TREAT-NMD Member at treat-nmd.eu/membership
- Sign up for the TREAT-NMD Newsletter at treat-nmd.eu/newsletters
- Visit the TREAT-NMD Website (treat-nmd.eu)
- Conferences/Education – find out more about upcoming events at treat-nmd.eu/conferences

Patient Organisation Representatives and Registry curators – Are you a member of the TREAT-NMD Global Database Oversight Committee (TGDOC)?

Did you know if you are funding clinical research you can make use of TACT (TREAT-NMD Advisory Committee for Therapeutics) and other TREAT-NMD tools?

Contact us

If you would like to find out more about TREAT-NMD please contact:

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