Welcome to the tenth GNE Myopathy Disease Monitoring Programme (GNEM-DMP) newsletter and thank you for your continued support and participation. This newsletter is intended to provide you with regular updates of the registry and other GNE myopathy related topics. We welcome your feedback and suggestions on this newsletter.

This Newsletter Features:

Update on registry statistics

Results of the registry's first academic research paper

Research and scientific conference update

Message from Ultragenyx and future changes to the registry

A warm welcome to all of the new registry members

To join the GNE Patient Registry please visit: www.gnem-dmp.com

Contact us at: gnem@treat-nmd.eu
We are very pleased to report that in spite of the language barriers, the GNE Myopathy registry enters the year 2018 with 354 participants from 36 countries, spanning 6 continents (Fig 1). It remains an important and valuable part of the research field and patient community, its existence will continue to meet the need for the disease awareness and translational research in 2018. We want to say a BIG thank you to each of you who have registered and provided information about how GNE Myopathy affects you. By providing this information you are enabling scientists to better understand how the disease progresses over a long period of time. In essence the more details you provide the better scientists can understand GNE Myopathy. Every answer counts.

Fig. 1. Countries in the green colour shows the geographical spread of people with GNE Myopathy who are registered to the GNEM-DMP.

The answers you have provided to the registry so far have recently been carefully analysed and summarised by Dr O Pogoryelova and a team of GNE Myopathy experts from around the world. The results have been published in the form of a scientific paper. This is the first academic paper using the registry data and a great example of how the information you provide is being used to inform the scientific community. The full version is available here: https://goo.gl/Rhoia4

To allow scientists and doctors to carry on analysing the registry data and plan further research in GNE Myopathy we want to encourage you all to keep completing your annual questionnaires. If you have not completed one in 2017 please get in touch with us or login here www.gnem-dmp.com. The questionnaires take around 15-20 minutes to complete. 41% of participants (Fig 2) completed their second year questionnaires, If you can think of ways we could help improve this, please let us know.

Patient advocacy groups remain critical to educating and raising awareness in the GNE Myopathy field and it was great to see so many being held in 2017: Israel, Italy (Gli Equilibri HIBM), USA (Neuromuscular Disease Foundation, Ultragenyx), and International (GM GNE Myopathy International). We’d like to thank those who provided information about the registry to your attendees. Contact details of the different patient advocacy groups are provided at the end of the newsletter.

Fig. 2. The number of registry participants who completed their 2nd year questionnaire.
Dr. Pogoryelova from Newcastle University and a number of neuromuscular experts have been working together to analyse the registry data to try and understand the clinical presentation and severity of the disease. We are proud to say this paper was recently accepted for publication in Neuromuscular Disorders Journal. Below is an infographic of the paper and its main findings.

**Paper Title:** Phenotypic stratification and genotype correlation in a heterogeneous, international cohort of GNE Myopathy patients: First report from the GNE myopathy Disease Monitoring Program, registry portion

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**What registry data was included in analysis?**

- **GNEM-FAS data from 150 participants** was included
- **26 countries were represented**
- **Iran, Italy, South Korea, USA, UK** and **India** represent **77.7% of all participants who answered questionnaires**
- **48% are male**
- **52% are female**

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**Key Findings**

**Onset & Diagnosis**
- Mean age of onset is **27.8 years**
- Females had an earlier onset than Males (F=26.5 years vs M= 29.2 years)
- Average age of diagnosis is **32.7 years**
- It takes on average **5.2 years for a diagnosis**

**First Symptoms**
- Symptoms affecting lower extremity weakness is present in most patients, manifesting at around 28.8 years
- Weakness in arms and hands was reported on average 4 years later

**Ambulation Status**
- 24.3% of registry population were non-ambulant at baseline assessment
- 36.4% of ALL respondents reported using wheelchair for long journeys
- For wheelchair users it took 11.9 years from onset until a wheelchair was required (range: 5- 25 years)
- The mean age of registry participants who use a wheelchair is 38.3 years

**Genetic Mutation Type & Disease Severity**
- Mutation specific analysis in this cohort demonstrated a genotype-phenotype relationship i.e. those with p.Ala662Val mutation may be associated with a more severe phenotype than those with p.Val727Met

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**Conclusions**

The registry is a versatile tool for disseminating information and also for recruitment to clinical trials. This patient reported data showing disease presentation and progression support previous retrospective reports of GNE myopathy. Acknowledging the study limitations these observational findings need to be replicated in a larger cohort before conclusions can be drawn. The registry continues to evolve and collect data on a large international population over a long period of time. It continues to address scientific difficulties and help research from drug development to clinical care.
Engagement Activities

The team here at Newcastle University have been involved in many scientific activities to raise awareness of GNE myopathy since our last update in the previous newsletter.

World Muscle Society.... GNEM-DMP Poster

In early October 2017 the World Muscle Society (WMS) held its 22nd International Annual Congress in St Malo, France. WMS is arguably one of the largest neuromuscular conferences and is attended by esteemed and young physicians, researchers, therapists and neuropathologists from around the world. It provides us with a great opportunity to raise awareness, particularly about rare conditions like GNE myopathy. The conference was well represented by Newcastle University staff Dr Pogoryelova attended. We were very pleased Dr Pogoryelova was provided with the opportunity to inform congress about GNE Myopathy by being selected to display a poster: ‘Genotype-phenotype correlation analysis in GNE myopathy’. The poster was well received and generated lots of discussion. There were a number of other International academic institutes also displaying posters about GNE myopathy; National Institute of Health (NIH, USA), National Centre of Neurology and Psychiatry (NCNP, Japan), CHU de la Reunion (Africa) and finally, Egypt Air Hospital. It is clear the range of scientific investigations being carried out in the area of GNE myopathy is varied. Topics ranged from investigations using mouse models to examine biochemical pathways in relation to sialic acid biosynthesis, registries, case studies and genotype - phenotype analyses.

Treat-NMD

The 5th International Treat-NMD Conference was held in Freiburg November 2017. Over 200 neuromuscular clinicians, experts, stakeholders and patient representatives attended the conference. The aim was to share lessons learned in the area of translational medicine for neuromuscular diseases and plan for the delivery of future therapies to patients. There was an exciting range of speakers, topics discussed included: the tools and resources needed to run efficient clinical trials, standardised approaches to developing patient registries, improving standards of care, and improving assessments in preclinical models of neuromuscular disease.

Key Poster Points

The aim was to analyse clinical outcomes to see if there was a correlation between the type of mutation and disease severity.

Participants who had provided their genetic report were included in the analyses (n=278)

Further research is needed to determine conclusively
Changes to the registry

Withdrawal of Ultragenyx

As you may have heard, last August, Ultragenyx Pharmaceutical Inc. (Ultragenyx) announced that a Phase 3 study evaluating aceneuramic acid extended release (Ace-ER) in patients with GNE Myopathy did not achieve its primary and some secondary research endpoints. As a result, Ultragenyx decided and announced that it would discontinue further clinical development of Ace-ER. A letter to patients from our CEO, Emil Kakkis, followed the initial announcement. A link to that letter can be found here.

In the months that followed that announcement, Ultragenyx started the long process of winding down the clinical studies and programs which supported the development of Ace-ER, all the while keeping the needs of patients in mind. Part of that wind-down included exploring options for keeping the Disease Monitoring Program going. Though the in-clinic portion of the Disease Monitoring Program will discontinue, TREAT-NMD (http://www.treat-nmd.eu/), which ran the online GNEM DMP in accordance with Ultragenyx’s study guidelines, has agreed to assume full responsibility for the online program, so it can continue under a TREAT-NMD study plan. Therefore, as of March 1, 2018, Ultragenyx will no longer be responsible for or involved in the online program, and TREAT-NMD will take over all aspects of it.

This change in ownership should not greatly affect you as a participant in the online program. The interface and system will look almost identical to what you currently see. The one big difference is that the Ultragenyx logo will no longer be listed anywhere on the website. You will also need to sign a TREAT-NMD consent to participate in TREAT-NMD’s study.

Both TREAT-NMD and Ultragenyx are hopeful that TREAT-NMD’s study will with continue to expand both awareness and understanding of GNE Myopathy. If you have any questions about this transition or what it means to you, feel free to contact the GNE registry curator at hibm@treat-nmd.eu.
Since the closure of the Phase 3 randomised, Double-Blind, Placebo-Controlled Study to evaluate Sialic acid in people with GNE Myopathy and subsequently the increased attention on sialic acid as a nutritional supplement, we have received questions from participants enquiring as to whether they should increase their dietary intake of sialic acid. This is a topic we discussed in a previous newsletter (Issue 3) found at: www.gne-registry.org. The scientific literature remains the same.

- Sialic acid is most naturally found in milk serum at around 1.68 -3.93g/kg (depending on cattle breed)
- No research has been conducted to determine the effect of dietary sialic acid products on muscle function in patients with GNE Myopathy
- The authors of the original article could see no harm in enjoying a well-balanced diet which has high sialic acid content but the short term and long term benefits are not known

Get Involved

We are looking for new fresh ideas for the gnem-dmp registry newsletter. Please let us know what you would like to see included in the newsletters. If you have anything you would like to share in the newsletter then please let us know at HIBM@treat-nmd.eu

Help with Translations

We are also looking for volunteers to help with future newsletter translations in Arabic, Chinese, Dutch, Farsi, French, German, Hebrew, Italian, Korean, Portuguese, Spanish and Turkish. If you have the time and are able to help with this then please get in touch HIBM@treat-nmd.eu

Patient Organisations

Below is a list of patient organisations and support groups which include GNE myopathy and Muscular Dystrophy internationally

USA
Neuromuscular Disease Foundation
www.cureHIBM.org

UK
Muscular Dystrophy UK
www.musculardystrophyuk.org

Italy
Associazione Gli Equilibristi HIBM
www.gliequilibristsi-hibm.org

Japan
Distal Muscular Dystrophy Patients Association
www.enigate.com

International
Advancement of Research for Myopathies
www.hibm.org

International
GNE Myopathy International
www.gne-myopathy.org

International
(Sephardic & Mizrahi Jewish Communities)
Sephardic Health Organisation for referral and Education
www.shoreforlife.org

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