HEREDITARY NEUROPATHY FOUNDATION

cmtupdate

Impact That Matters

Driving CMT Research with the Patient's Voice

SUMMER 2023

The time is NOW to participate in CMT research.

CMT Genie

Despite the best efforts of our CMT community providing resources to obtain genetic testing, there are still barriers that remain challenging in obtaining a definitive diagnosis. HNF has changed that by developing the CMT Genie program. We are here to support and facilitate genetic counseling and provide immediate access to information and support for in-home testing and the translation of genetic reports to patients. Whether you need to learn more about variants identified in your DNA or seek further explanation of inheritance patterns, the CMT Genie is available to all patients and families affected by CMT, and for those that suspect CMT is the cause of their symptoms.

Book a CMT Genie Call
tinyurl.com/4d75xu45

"The process was very easy. I met with Genome Medical and received the genetic test kit within a few days. The kit was well packaged in a small box and had everything I needed. Shortly after I shipped the kit back, I received an email to register online. Less than two weeks later, I received my test results – CMT1A, just as I suspected. Genome Medical notified me via text and email about scheduling a follow-up appointment to go over the results."

— Carrie H.

"I got the results which were negative. I am glad I did the testing, so I now know more than I did before about genetic variants I do not have. Kind of like Thomas Edison and his search for a filament for a light bulb."

— Jeff M.

CMT UPDATE
SUMMER 2023

Allison T. Moore
Founder and CEO
Hereditary Neuropathy
Foundation

Dear CMT Community,

How's your summer going so far? I am happy to be back home after traveling to Europe to represent the Patient Voice at three major CMT meetings: European CMT Federation (ECMTF) meeting, EuroMit 2023 and the annual Peripheral Nerve Society Annual Meeting (PNS). I hope you all find these meetings and the increased interest in investigating and treating ALL types of CMT as encouraging as I do! We all know that CMT is rare, so we need to pull together to collect and share crucial data about the lived CMT experience to get the interest of researchers and drug developers. And that's exactly why HNF's primary focus is to continue to improve and expand on the data we collect in our Global Registry for Inherited Neuropathies, GRIN, and to get every one of you genetically tested for CMT so that we can accurately characterize the various subtypes of CMT and make sure you are ready for clinical trials WHEN they happen.

I am so excited to be able to share this latest CMT Update with you! You'll be able to read about some of the valuable information that is already available from GRIN. Dr. Florian Thomas and his team at Hackensack Meridian Health in New Jersey presented a poster at the PNS meeting featuring pain and CMT. Please note: they pointed out that a genetic diagnosis is important in the data collection and analysis, so please consider using our CMT Genie program (www.cmtgenie.org) if you don't already have a genetic diagnosis, or if you were tested over five years ago and didn't get an answer at that time. If you have a genetic test report, please take just 5 minutes to upload it into your secure GRIN portal in the Documents section today (or email registrycoordinator@hnf-cure.org for instructions).

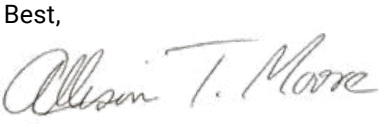
Another study of GRIN data is detailed in this CMT Update, as well. This time, a team led by Brian J. Piper, PhD and Gregory T. Carter, MD, used GRIN data to evaluate different aspects of cannabis use for the management of pain and CMT. I think you'll find their analysis interesting and I hope that you'll take the Medical Cannabis survey in GRIN so that we can collect even more supportive data on this topic.

We all know that CMT starts in infancy. The symptoms may take awhile to present themselves and the disease may not be readily apparent, but as you'll read on page 7, one of the most common first signs of CMT in the pediatric years - in both CMT Type 1 and 2 - is weak ankles and an abnormal gait. HNF thanks the wonderful team at Connecticut Children's for publishing their work on this topic. HNF continues to prioritize the need for early CMT interventions and will be announcing an exciting new opportunity for kids to participate in a research study in preparation for pediatric clinical trials this fall. Please register your child in GRIN today to make sure you are notified of this opportunity! For more information from HNF about Pediatrics and CMT, please visit this dedicated Pediatrics and CMT section on our website.

In addition to collecting important information for research, GRIN is the only IRB-approved CMT patient registry in the WORLD that collects and shares de-identified information critical to ourTRIAD pharma partners for developing successful clinical trials. For exciting updates from four pharma and biotech companies, please don't miss the latest news from Applied Therapeutics, Pharnext and NMD Pharma and DTx Pharma in this *CMT Update*. If you've already joined GRIN, you may have already received these updates. If you would like to be notified immediately about drug development in the CMT field, don't wait – join GRIN today.

I hope you will value the information in this CMT Update and I look forward to hearing from you with any feedback, questions or ideas. With all of the current positive research momentum, there is no better time than right now to support HNF! Become a part of the effort to find the treatments and cures for all Inherited Neuropathies by donating today. As always, I appreciate your support of the HNF mission and its programs.

Best,



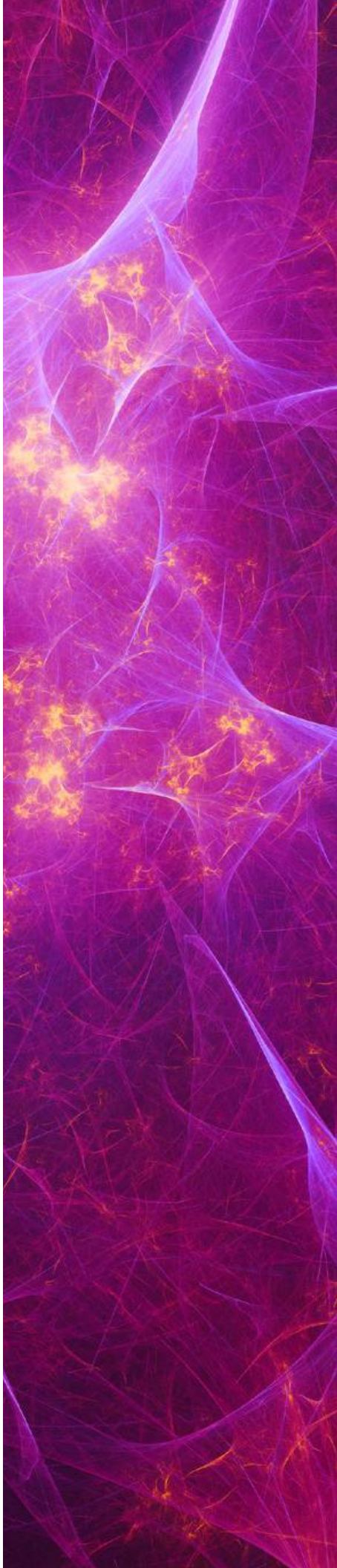
Allison T. Moore

GLOBAL REGISTRY FOR INHERITED NEUROPATHIES

9 KEY FINDINGS FROM YOUR GRIN SURVEYS (AND WHY YOU NEED TO COME BACK AND COMPLETE MORE)

In June, CMT researchers, clinicians, industry leaders and patient advocacy group leaders met in Copenhagen, Denmark for the annual Peripheral Nerve Society meeting. The Hereditary Neuropathy Foundation's Global Registry for Inherited Neuropathies (GRIN) was the center of attention during the poster presentation by the team at Hackensack Meridian Health.

Their study aimed to evaluate the impact of neuropathic pain on the psychosocial well-being of individuals with Charcot-Marie-Tooth (CMT) disease, a hereditary neuropathy. In summary, this study highlights the significant impact of neuropathic pain on the quality of life and psychosocial well-being of individuals with CMT. It also emphasizes the importance of addressing pain management strategies and promoting interprofessional care to improve patient outcomes.



Here are the key findings and conclusions:

1. **Neuropathic Pain in CMT:** The majority of patients with CMT experience mild to moderate neuropathic pain at least once per week. Neuropathic pain was found to be a significant contributor to the disease burden reported by patients.

2. **Pain Severity and Quality of Life:** Pain severity was associated with diminished life satisfaction and increased social isolation. Participants with more severe, neuropathic-type pain reported lower life satisfaction and higher levels of social isolation. Life satisfaction scores decreased with increasing pain severity.

3. **Exercise Engagement:** Participants with pain reported lower engagement in daily exercise compared to those without pain. Respondents with pain reported 10% lower engagement in more than 30 minutes of daily exercise.

4. **Opioid Use:** High rates of opioid use for neuropathic pain were observed among the survey population, with 27.2% of patients reporting the use of opioids. This highlights the need for education and awareness regarding evidence-based pain treatment options.

5. **Interprofessional Treatment:** The study suggests that interprofessional treatment of neuropathic pain may improve both psychosocial and physical outcomes in individuals with CMT.

6. **Gender and Pain:** Females younger than 65 years old reported more severe pain compared to females older than 65 and males in both age groups.

7. **Prevalence of Neuropathic Pain:** The majority of respondents (63.95%) experienced neuropathic-type pain based on the generated T-scores.

8. **Study Limitations:** The self-reported diagnoses of CMT were not confirmed with genetic reports, potentially including individuals with misdiagnosed CMT in the study population.

9. **Future Directions:** A second generation of the Global Registry for Inherited Neuropathies (GRIN) was commissioned to acquire more genetic reports, allowing for diagnostic confirmation and stratification by CMT subtype.

10. **The time is NOW to participate in CMT Research by completing the three *NEW* GRIN Surveys:** Natural History Survey v2 + Lifestyle Survey + Medication Survey

View poster: Click here!

HNF is happy to announce that the Global Registry for Inherited Neuropathies Natural History Study for Charcot-Marie-Tooth is now listed at clincialtrials.gov.

ClinicalTrials.gov Identifier: NCT05902351

Using Medical Cannabis for Managing Pain in Charcot-Marie-Tooth Disease — Patient Reported Outcomes

Data regarding medical cannabis use for pain relief in CMT from HNF's CMT Patient Registry, GRIN, was analyzed and published by a team led by Brian J. Piper, PhD and Gregory T. Carter, MD. The results revealed the vast majority of those surveyed experienced significant relief, providing evidence that controlled trials are needed to evaluate this pain treatment in CMT further.

Chronic pain is a major problem for patients with CMT disease.

This exploratory study examined patient reported efficacy of medical cannabis for pain management in this population. Participants were recruited through the Hereditary Neuropathy Foundation and the Global Registry for Inherited Neuropathies (GRIN). The online survey contained 52 multiple choice questions about demographics, medical cannabis use, symptoms, efficacy, and adverse effects. Nearly all (90.9%) of respondents reported experiencing pain, including all (100%) females and 72.7% of males with 91.7% of respondents indicating cannabis provided at least 50% pain relief. **The most frequent response was an 80% reduction in pain**. Moreover, 80% of respondents reported using less opiates, 69% noted using less sleep medication, and 50% reported using less anxiety/antidepressant medications. Negative side effects were noted by 23.5% of respondents. However, almost all of that subgroup did not have plans to stop consuming cannabis. One-third possessed a medical cannabis certificate. Patient perceptions of their physicians' attitudes regarding patient medical cannabis use greatly impacted whether respondents informed their providers of their usage. The vast majority of patients with CMT reported that cannabis was effective to manage pain symptoms. The data support the need for prospective, randomized, controlled trials using standardized dosing protocols to further delineate and optimize the potential use of cannabis to treat pain related to CMT.

Cannabis Patient Resources:
Click Here!

• • • • •

Read the Publication:
Click Here!

• • • • •

Participate in valuable CMT research by joining GRIN today!

Join GRIN:
Click Here!

GLOBAL REGISTRY FOR INHERITED NEUROPATHIES

HNF TRIAD ACADEMIC PARTNER CONNECTICUT CHILDREN'S PUBLISHES RESULTS OF CMT PEDIATRIC NATURAL HISTORY STUDY TO BETTER UNDERSTAND ANKLE FUNCTION AND GAIT

HNF-funded research sought to determine how age and CMT type affect ankle strength in children. A detailed understanding of neuropathy progression is needed to guide informed treatments to improve or prevent a decline in gait function.

Gait analysis and range of motion strength testing were used to evaluate children with both CMT1 and CMT2. The children with CMT1 had slightly more ankle strength that continued to increase with age until it plateaued at about 13 years, while the children with CMT2 were weaker and plateaued earlier but did not seem to get weaker with age. This highlights the importance of having an in-depth understanding of gait at the individual patient level using comprehensive gait analysis, including valid and reliable strength measures. HNF continues to fund critical Pediatric Natural History Studies for CMT in preparation for clinical trials and to improve treatment outcomes.

ARE YOU A PARENT/CAREGIVER OF A CHILD WITH CMT?

Please participate in pediatric CMT research by joining today!

Join GRIN: Click Here!

JOIN GRIN

Turn CMT Symptoms into Science

50
Countries Represented

3704
Participants

41
Types of CMT Represented

CLINICAL TRIAL WILLINGNESS

44%
Gene Therapy

38%
Investigational Drugs

47%
Activity Monitoring (wearable)

Click!

JOIN GRIN

Great News From Two HNF TRIAD Industry Partners — Applied Therapeutics & Pharnext

Applied Therapeutics, Inc. has announced that their drug candidate, AT-007 (Govorestat), has received orphan medicinal product designation from the European Medicines Agency (EMA) for the treatment of Sorbitol Dehydrogenase (SORD) Deficiency. This designation reflects the high unmet medical need in SORD Deficiency and recognizes the benefit of Govorestat in reducing toxic sorbitol levels. New data published in the Journal of Clinical Investigation has further explained the molecular pathophysiology of SORD neuropathy and the role of sorbitol in neuronal toxicity. This is an important step for advancing regulatory initiatives in Europe and provides certain benefits and incentives for the development and marketing of the medicine.

Press Release: Click here!

Pharnext, a biopharmaceutical company, has announced new positive results from the ongoing open-label extension study of their drug PXT3003 in Charcot-Marie-Tooth Disease Type 1A (CMT1A), called the PLEO-CMT-FU trial. The trial has been conducted for a total of 6 years, and the data is consistent with a long-term treatment benefit of PXT3003 in patients with mild-to-moderate CMT1A. The results indicate that PXT3003 has a good safety profile and shows a long-term treatment effect on the Overall Neuropathy Limitation Scale (ONLS), which measures functional motor disability. A group of 117 patients with mild-to-moderate CMT1A are still receiving treatment with the high dose of PXT3003 in the trial.

Press Release: Click here!

Significant New Findings

Shared by NMD Pharma at the Peripheral Nerve Society Annual Meeting (PNS) in Copenhagen, Denmark

NMD Pharma A/S is a clinical stage biotech company focused on developing small molecule ClC-1 inhibitors for neuromuscular disorders. They presented the results from their observational study called ESTABLISH1 at the Peripheral Nerve Society Annual Meeting (PNS) in Copenhagen, Denmark.

These findings are significant as they provide new insights into the understanding of CMT types 1 and 2 and may contribute to the development of future treatments for these inherited neurological conditions.

The study identified a new disease characteristic in patients with CMT types 1 and 2, which is a neuromuscular junction (NMJ) transmission deficit. The severity of the NMJ transmission deficit was associated with disease severity, as measured through various clinical assessments of muscle strength and function.

The international study was led by Dr. Henning Andersen from Aarhus University Hospital and Dr. William David Arnold from NextGen Precision Health, University of Missouri. The study compared electrophysiological assessments (single fiber electromyography and repetitive nerve stimulation) and clinical testing (including tests of muscle strength, fatigability, dexterity, and balance) between 21 patients with CMT types 1 and 2 and 10 healthy age-matched subjects. The study also provided important information about the tolerability and reliability of clinical and electrophysiological outcomes, which will help in selecting relevant outcomes for future clinical trials.

Additional information about the study can be found on the clinicaltrials.gov website using the identifier NCT04980807.

TRIAD

BREAKING NEWS

DTx Pharma Receives FDA Orphan Drug Designation for DTx-1252 for the Treatment of Charcot-Marie-Tooth Disease Type 1A (CMT1A)

DTx Pharma, a biotechnology company addressing the delivery challenges of oligonucleotide therapeutics with its Fatty Acid Ligand Conjugated OligoNucleotides (FALCON™) platform, today announced that the FDA has granted Orphan Drug Designation to DTx-1252, an investigational FALCON small interfering RNA (siRNA) therapeutic for the treatment of Charcot-Marie-Tooth Disease Type 1A (CMT1A).

About FDA Orphan Drug Status

Orphan Drug status refers to a special designation granted to pharmaceutical products that are developed to treat rare diseases or conditions. In many countries, including the United States, the European Union, and Japan, orphan drug status provides certain incentives and benefits to pharmaceutical companies to encourage the development of therapies for rare diseases.

These incentives may include extended market exclusivity, tax credits, fee waivers, and assistance with the drug approval process. The intention is to promote the development of treatments for diseases that affect a relatively small number of people and may not be financially viable for pharmaceutical companies to pursue without such incentives.

To qualify for orphan drug status, a medication must meet specific criteria defined by regulatory authorities, such as having a prevalence below a certain threshold in the population. Once granted orphan drug status, the pharmaceutical company may receive assistance and incentives to facilitate the development and commercialization of the drug, ultimately benefiting patients with rare diseases.

DTX PHARMA

About DTx-1252

DTx-1252 is a potential first-in-class FALCON™ siRNA therapeutic for treatment of CMT1A. By repressing PMP22, DTx-1252 reverses CMT1A in a mouse model that faithfully recapitulates the genetic and clinical manifestations of the disease. DTx-1252 treatment induces remyelination of axons to normal levels, improves relevant electrophysiological measurements and increases muscle mass, grip strength, coordination and agility in preclinical studies.

IMPORTANT STEPS TO TAKE

If you have a confirmed genetic diagnosis of CMT1A, now is the time to make sure you are in HNF's Global Registry for Inherited Neuropathies and upload your genetic report.
Join GRIN

If you do not have a confirmed genetic diagnosis of CMT1A, now is the time to make an appointment with the CMT Genie to pursue a genetic diagnosis.
Make an appointment with the CMT Genie

HNF
1641 3rd Avenue
#28K
New York, NY 10128
hnf-cure.org

DONATE!
Click Here!

Learn more about HNF resources

Visit hnf-cure.org
to learn more about:

- Movement is Medicine™
- CMT-Connect Webinars
- HNF Centers of Excellence
- The CMT Genie
- Join Team CMT
- Patient Resources

Global Registry for Inherited Neuropathies (GRIN):

A Patient-Powered Registry Boosts the Study of Charcot-Marie-Tooth (CMT) Disease

CMT is a genetic, degenerative neuromuscular disease that affects 1:2500 in the US and 2.5 million worldwide—many are still undiagnosed—and currently, there is no cure. CMT is progressive, and over time, muscles in the feet, legs, and hands lose strength. Muscles waste away and cause atrophy leading to mobility issues. It can have a serious impact on vision, hearing, breathing, speech, and swallowing in extreme cases. Some patients experience hip dysplasia, scoliosis, and/or blindness.

MISSION:
Global Registry for Inherited Neuropathies (GRIN) was developed to conduct patient-focused research and for the development of treatments and cures for Charcot-Marie-Tooth (CMT). GRIN is the only comprehensive patient registry collecting patient-reported information about living with CMT in combination with genetic reports, electronic health records, and other critical data for research. The patient voice is at the forefront of all we do.

The Hereditary Neuropathy Foundation mission is to increase awareness and accurate diagnosis of Charcot-Marie-Tooth (CMT) and related inherited neuropathies, support people living with CMT and their families with critical information to improve quality of life, and fund research that will lead to treatments and cures.

www.hnf-cure.org

Publication of this newsletter was made possible with the financial support of Pharnext.