Second European CMT Specialists Conference

PUBLICATIONS/READINGS:

Running and Planned Clinical Trials (Tim Vangansewinkel) M13 / WP 5

Plenary Session 4: Clinical trials, data sharing and outcome measurement

Literature

Overview preclinical research and ongoing clinical trials
https://cmtrf.org/research/cmt-research-pipeline/

Review: Charcot-Marie-Tooth disease: a review of clinical developments and its management - What's new in 2025?
https://www.tandfonline.com/doi/epdf/10.1080/14737175.2025.2470980?needAccess=true

List of ongoing clinical trials and literature references

1. **Applied Therapeutics**
   INSPIRE Trial, NCT05397665
   Govorestat
   Aldose reductase inhibitor
   People with SORD deficiency (CMT-SORD)
   Phase II/III

https://www.appliedtherapeutics.com/pipeline/govorestat/
Cortese et al. Genotype and phenotype spectrum of Charcot-Marie-Tooth disease due to mutations in SORD. 2025. BRAIN https://academic.oup.com/brain/advance-article/doi/10.1093/brain/awaf021/8010720

2. **UCL Queen Square centre for neuromuscular disorders**
   SENSE trial, NCT06113055
   HSN1 (Hereditary Sensory Neuropathy)
   SPTLC1 or SPTLC2 mutations
   L-Serine (amino acid therapy)
   Phase II
   https://cmtausa.org/research-projects/hereditary-sensory-neuropathy-serine-trial-sense-trial/
   Garofalo et al. Oral L-serine supplementation reduces production of neurotoxic deoxysphingolipids in mice and humans with hereditary sensory autonomic neuropathy type 1. 2011. Journal of Clinical Investigation https://pubmed.ncbi.nlm.nih.gov/22045570/

3. **NMD Pharma®**
   SYNAPSE-CMT, NCT06482437
   NMD670
   ClC-1 – chloride channel modulator
   CMT1 and CMT2 patients
   Phase IIa
   https://www.nmdpharma.com/news/nmd-pharma-initiates-phase-2-study-of-nmd670-in-patients-with-cmt-type-1-and-2
   Skjærlund Grønnebæk et al. Neuromuscular transmission deficits in patients with CMT and ClC-1 inhibition in CMT animal models. 2024. Ann Clin Transl Neurol. https://onlinelibrary.wiley.com/doi/epdf/10.1002/acn3.52252

4. **Inflectis BioScience**
   IFB-088 (Sephin1)
   Proteastasis modulator (inhibition dephosphorylation of eIF2α
   CMT1A, 1B, 1E
   Phase I
   https://inflectisbioscience.com/our-pipeline/
   Bai et al. Treatment with IFB-088 Improves Neuropathy in CMT1A and CMT1B Mice. 2020. Mol Neurobiol. https://link.springer.com/article/10.1007/s12035-022-02838-y

5. **Augustine Therapeutics**
   AGT-100216
   HDAC 6 inhibitor, peripherally selective
   CMT1 and CMT2 (broad potential)
   Phase I (healthy adults, CMT patients next)
   https://www.augustinetx.com/pipeline
   https://www.augustinetx.com/media/augustine-therapeutics-announces-first-patient-dosed-in-phase-i-clinical-trial-evaluating-lead-candidate-agt-100216-for-the-treatment-of-charcot-marie-tooth-disease
   Rossaert and Van Den Bosch, HDAC6 inhibitors: Translating genetic and molecular insights into a therapy for axonal CMT. 2020. Brain Research. https://www.sciencedirect.com/science/article/pii/S0006899320300482?via%3Dihub

Benoy et al. Development of Improved HDAC6 Inhibitors as Pharmacological Therapy for Axonal Charcot–Marie–Tooth Disease. 2017. Neurotherapeutics. https://www.neurotherapeuticsjournal.org/article/S1878-7479(23)01476-9/fulltext
d'Ydewalle et al. 2011 HDAC6 inhibitors reverse axonal loss in a mouse model of mutant HSPB1-induced Charcot-Marie-Tooth disease. 2011. Nature medicine. https://www.nature.com/articles/nm.2396

6. **CKD Pharmaceuticals (Novartis)**
   CKD-510
   HDAC6 inhibitor
   CMT1 and CMT2
   Phase I

7. **Actio Biosciences**
   ABS-0871
   TRPV4 ion channel inhibitor
   CMT2C (TRPV4 mutation)
   Phase I
   https://actiobiosciences.com/actio-biosciences-announces-first-participant-dosed-in-phase-1-clinical-trial-of-abs-0871-a-novel-trpv4-inhibitor-for-the-treatment-of-charcot-marie-tooth-disease-2c/

8. **VANDA Pharmaceuticals inc.**
   VCA-894A
   Antisense oligonucleotide
   CMT2S (IGHMBP2 mutation) – custom for one patient
   Phase I (first dose administered June 2025)

9. **ENCell**
   EN001
   allogeneic Wharton's jelly mesenchymal stem cell therapy (IV infusion)
   CMT1A
   Phase I → Ib
   https://www.encellinc.com/en/sub/rnd/pipeline.asp
   Report on its use in Duchenne Muscular Dystrophy (phase I trial):
   https://thejcn.com/DOIx.php?id=10.3988/jcn.2024.0299

10. **Orthogonal Neuroscience**
    ORT247
    mAb inhibitor of EphA4 receptors
    CMT1 and CMT2

11. **Helixmith**
    Engensis (VM202), NCT05361031
    Phase I/IIa
    CMT1A
    Plasmid DNA expressing two isoforms of hepatocyte growth factor
    https://www.helixmith.com/eng/s2/s2_1_1_5.php
    https://www.clinicaltrials.gov/study/NCT05361031?term=AREA%5BBasicSearch%5D(vm202)&rank=6

12. **Alcyone Therapeutics**
    ACTX technology
    Gene replacement - AAV9 vector carrying the IGHMBP2 gene
    Phase I/IIa
    CMT2S
    https://www.clinicaltrials.gov/study/NCT05152823

13. **Pharnext S.C.A.**
    PREMIER - NCT04762758
    PXT3003 - baclofen, naltrexone hydrochloride [HCl], and D-sorbitol
    CMT1A
    Phase III, trial ended
    https://clinicaltrials.gov/study/NCT04762758
    Chumakov et al. Polytherapy with a combination of three repurposed drugs (PXT3003) down-regulates Pmp22 over-expression and improves myelination, axonal and functional parameters in models of CMT1A neuropathy. 2014. Orphanet J Rare Dis. https://pmc.ncbi.nlm.nih.gov/articles/PMC4279797/

14. **Novartis (DTx Pharma)**
    DTx-1252
    Preclinical phase → IND planned
    siRNA targeting PMP22
    https://www.novartis.com/news/media-releases/novartis-builds-neuroscience-pipeline-and-xrna-platform-capabilities-acquisition-dtx-pharma

We are most grateful for the generous support of this Conference by:

Flanders State of the Art
Co-funded by the European Union
APPLIED THERAPEUTICS
fwo
AFMTÉLÉTHON CURE THROUGH INNOVATION