Deliverable D.2.2.

Model CMT online training program / seminar

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Introduction

CMT is the most common form of inherited neuropathies, with a prevalence of 1 : 2500 (1); it is often not or poorly mentioned in medical school training programs, throughout Europe. Given the high number of rare diseases (around 8.000) it cannot be a priority in medical school programs, thus, many physicians, even neurologist, are not familiar with its symptoms. CMT is also virtually unknown in the general public, and media do not deal with it. People affected by CMT, thus, have difficulties to find the proper physician, and the average diagnostic odyssey is around 10 years (2). As explained in Deliverable D.2.1 there is a need for additional medical training resources. Online courses and seminars can help to improve the situation and the living conditions of the people affected.

On this basis, with reference to the materials and literature listed below, and as a basis for further discussion and elaboration, we herewith launch a model online training program/seminar for CMT. It is open for discussion and will have to be more elaborated over time. Given expected achievements of research in the field, regular updates are also inevitable. The European CMT Research Association (ECRA) was created to further advance research and development, and with the 2nd European CMT Specialists Conference (EUCMTSC) the process has got new momentum. More materials are available on the ECRA website at the “research” rubric and can be found, in particular under “topics&projects” (https://ecra-np.org/topics-projects/), under “publications” (https://ecra-np.org/publications/) as well as under “education/training” (https://ecra-np.org/education-training/). Special links to video-takes of relevant presentations at the EUCMTSC are available on this website (https://ecra-np.org/conferences/2nd-eucmtsc-antwerp-23-25-october-2025/).

They are referred to infra under “materials and references” at the diverse sessions of the program outlined hereafter.

Model CMT online training program

Our model CMT online training program consists of 10 sessions, each taking 90 minutes with 30 minutes introduction by the lecturer and 30 minutes discussion on the key questions related to the subject matter. 15 minutes each are added before the introduction for an opening organizational section (1st session) or a short review/repetition of the preceding topics (session 2-12), and the discussion is followed by 15 minutes for a summary and critique of the session.

Session 1: Definition and epidemiology

- History: 140 years Charcot-Marie-Tooth
- Disease classification and prevalence
- Symptoms, typical natural history
- Pathomechanisms (overview)
- Inheritance

Materials and references:

- Overview: Burns, J., Timmerman, V., Laurá, M. *et al*. Charcot–Marie–Tooth disease and related neuropathies. *Nat Rev Dis Primers* **12**, 3 (2026), https://www.nature.com/articles/s41572-025-00679-2

Session 2: Clinical diagnostics

- Medical history of the patient, family history
- Neurological examination
- Nerve conduction studies
- Differential diagnosis
- Perspectives for AI based diagnostics (D 3.2)

Materials and references:

- EUCMTSC Quartesan: Long-read sequencing reveals SORD/SORD2P inversions
- EUCMTSC W.M.Pernice: https://ecra-np.org/wp-content/uploads/2026/06/Health-data-management-and-the-use-of-AI-in-iNMD-diagnostics-Wolfgang-M.-Pernice.pdf
- Pareyson: https://ern-euro-nmd.eu/event/cmt-episode-1-challenges-in-the-diagnosis-and-treatment-of-inherited-neuropathies/
- Cortese: https://ern-euro-nmd.eu/event/cmt-episode-2-progress-in-genetic-diagnosis-for-neuropathies/
- Attarian: https://ern-euro-nmd.eu/event/diagnosis-of-charcot-marie-tooth-disease/

Session 3: Genetics

- Genetic diagnostic procedures
- Technologies for genetic testing
- Genetic classification and disease mechanisms
- Interpretation of genetic findings and variants of unknown significance
- Practical guidelines for genetic counseling

Materials and references:

- EUCMTSC: Advancing genetic diagnostics in CMT with long-read sequencing
- EUCMTSC: interview Cantarero/Reilly: https://www.youtube.com/watch?v=oaH-C5htxQE
- Kleopa: https://ern-euro-nmd.eu/event/gene-therapy/
- Record CJ, Skorupinska M, Laura M, Rossor AM, Pareyson D, Pisciotta C, Feely SME, Lloyd TE, Horvath R, Sadjadi R, Herrmann DN, Li J, Walk D, Yum SW, Lewis RA, Day J, Burns J, Finkel RS, Saporta MA, Ramchandren S,
- Weiss MD, Acsadi G, Fridman V, Muntoni F, Poh R, Polke JM, Zuchner S, Shy ME, Scherer SS, Reilly MM; Inherited Neuropathies Consortium—Rare Disease Clinical Research Network. Genetic analysis and natural history of Charcot-Marie-Tooth disease CMTX1 due to GJB1 variants. Brain. 2023 Oct 3;146(10):4336-4349. doi: 10.1093/brain/awad187. PMID: 37284795; PMCID: PMC10545504.
- Hoyle JC, Isfort MC, Roggenbuck J, Arnold WD. The genetics of Charcot-Marie-Tooth disease: current trends and future implications for diagnosis and management. Appl Clin Genet. 2015 Oct 19;8:235-43. doi: 10.2147/TACG.S69969. PMID: 26527893; PMCID: PMC4621202.

Session 4: Current therapeutic options - physiotherapy and rehabilitation

- General management and care, including symptomatic treatment, rehabilitation therapy
- Psychological care
- Towards Rehabilitation Guidance
- Aids, orthotics
- Pain management strategies

Materials and references:

- EUCMTSC d'Antonio et al.: https://ecra-np.org/topics-projects/towards-a-cure-of-cmt/
- EUCMTSC Ramdharry: Physical Management of CMT: Understanding Mechanisms
- EUCMTSC Schenone: Contribute of sensors, robots and AI in rehabilitation
- EUCMTSC Kleopa: Current status of therapeutics development for CMT neuropathies

Session 5: Orthopedic management and surgery

- Overview of surgical procedures and management option
- Foot surgery
- Tendon surgery
- Outcome measures
- Pratcical guidelines

Materials and references:

- Laurá M, Barnett J, Benfield J, Ramdharry GM, Welck MJ. Foot surgery for adults with Charcot-Marie-Tooth disease. Pract Neurol. 2024 Jul 16;24(4):275-284. doi: 10.1136/pn-2023-003825. PMID: 38631902.
- van der Wielen H, Nonnekes J, van Mierlo M, Donken CMA, Louwerens JWK, Keijsers NLW. Surgical correction of foot deformities in Charcot-Marie-Tooth-disease: effects on personal goals and gait capacity. Neuromuscul Disord. 2025 Oct;55:106213. doi: 10.1016/j.nmd.2025.106213. Epub 2025 Sep 3. PMID: 41032961.
- Ramdharry G, Singh D, Gray J, Kozyra D, Skorupinska M, Reilly MM, Laurá M. A prospective study on surgical management of foot deformities in Charcot Marie tooth disease. J Peripher Nerv Syst. 2021 Jun;26(2):187-192. doi: 10.1111/jns.12437. Epub 2021 Mar 13. PMID: 33650166.

Session 6: Pediatric management and transition

- General and special aspects of pediatric diagnostics
- Early-onset and severe subtypes: diagnostics
- Early-onset and severe subtypes: clinical management
- Transition procedures and challenges

Materials and references:

- Jani-Acsadi A, Ounpuu S, Pierz K, Acsadi G. Pediatric Charcot-Marie-Tooth disease. Pediatr Clin North Am. 2015 Jun;62(3):767-86. doi: 10.1016/j.pcl.2015.03.012. Epub 2015 Apr 15. PMID: 26022174.
- Yiu EM, Bray P, Baets J, Baker SK, Barisic N, de Valle K, Estilow T, Farrar MA, Finkel RS, Haberlová J, Kennedy RA, Moroni I, Nicholson GA, Ramchandren S, Reilly MM, Rose K, Shy ME, Siskind CE, Yum SW, Menezes MP, Ryan MM, Burns J. Clinical practice guideline for the management of paediatric Charcot-Marie-Tooth disease. J Neurol Neurosurg Psychiatry. 2022 May;93(5):530-538. doi: 10.1136/jnnp-2021-328483. Epub 2022 Feb 9. PMID: 35140138.

Session 7: Preclinical research models for studying pathomechanisms and for therapeutical approaches

- Preclinical animal models
- Stem cells and gene editing – a step beyond mouse models
- Genetic engineering (D 4.2)

Materials and references:

- EUCMTSC Cantarero: A new selective HDAC6 inhibitor ameliorates disease in a GDAP1 mouse

- EUCMTSC d'Antonio et al.: https://ecra-np.org/topics-projects/towards-a-cure-of-cmt/ D 4.2
- Previtali: https://ern-euro-nmd.eu/event/pathomechanisms-of-charcot-marie-tooth-disease/
- Kleopa: https://ern-euro-nmd.eu/event/cmt-episode-4-current-progress-in-charcot-marie-tooth-disease-cmt-treatments/
- Pareyson: https://ern-euro-nmd.eu/event/treatment-of-charcot-marie-tooth-disease/

Session 8: Clinical research for therapeutical approaches

- Drug development and clinical studies
- Disease modifying therapies
- Repurposing existing drugs (e.g., SORD)

Materials and references:

- EUCMTSC Fernandez: https://ecra-np.org/wp-content/uploads/2026/06/Recent-Therapeutical-Advances-for-CMT-Gorka-Fernandez.pdf
- EUCMTSC Raoss: Restoring PMP22 protein levels in CMT1A cells via base editing.
- EUCMTSC Kleopa: https://ecra-np.org/wp-content/uploads/2026/06/Genetic-and-other-Therapeutic-Approaches-Kleopas-Kleopa.pdf

Session 9: Assessment of CMT progress and outcomes of therapies

- Clinical outcome measures and hands-on use in clinical practice and research
- Biomarkers for measuring of disease progression
- Other and future tools to monitor disease course and response to treatment (D 5.1)
- AI-supported clinical outcome measures – new perspectives

Materials and references:

- Pareyson: https://ecra-np.org/wp-content/uploads/2026/06/Outcome-measurement-for-assessing-iNMD-therapies-and-the-effects-of-new-drugs-in-clinical-trials.pdf
- EUCMTSC Malby: Acetylated α-Tubulin as a clinical plasma biomarker
- Reilly: https://ern-euro-nmd.eu/event/cmt-episode-3-bioarkers-and-outcome-measures-for-clinical-trial-readiness-in-charcot-marie-tooth-disease-cmt/
- EUCMTSC Pareyson/Dohrn: Outcome measures for CMT and other neuromuscular disorders – utility and challenges (overview) D 5.1
- EUCMTSC W.M.Pernice: AI in CMT D 3.2

Session 10: Patients as Partners, digital care, and CMT in health policies

- The sleeping expertise of patients: the role of patient advocacy and self-support groups and patients as partners in research, drug development and clinical care
- Mobility of CMT patients and access to care: the facts, and application of telemedicine for digital care of CMT
- The socio-economic costs of CMT
- Raising awareness – activities of patient organisations and their impact

Materials and references:

- EUCMTSC I.Pernice et al.: Survey Report on Patient Readiness for Partnership in Research on inherited Neuromuscular Diseases
- EUCMTSC I.Pernice/F.Genovese: Cooperative Research & Development for a Cure of CMT – "patients as partners" D 6.2
- EUCMTSC Forsey: Patients as Partners in Research: The CMTA Experience
- EuCMTSC Leysen: Objectives and Visions of a Patient Organisation
- EUCMTSC H.F.Pernice: Digital Care: Challenges and Opportunities
- EUCMTSC Westhoven: Round Table: Access to therapy for patients with a rare disease
- EUCMTSC H.F.Pernice et al.: https://ecra-np.org/topics-projects/digital-care-strategy-for-cmt/
- EUCMTSC Stoykovic: https://ecra-np.org/wp-content/uploads/2026/06/Topical-publications-on-the-socioeconomic-Impact-of-CMT.pdf
- EUCMTSC Interview Leysen/Maltby: Patient readiness and recruitment for clinical trials
- Webinar Series: https://ecmtf.org/events/second-european-charcot-marie-tooth-specialists-conference/#:~:text=Program%20and%20Information-,Webinar%20Series,-In%20preparation%20for

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(1) Burns J, Timmerman V, Mukherjee-Clavin B, Yiu E, D'Antonio M, Laura M, Scherer SS, De Winter J. "Charcot-Marie-Tooth disease and related neuropathies" Nat Rev Dis Primers. 2026 Jan 22;12(1):3.

(2) Pernice HF, May S, Mühlensiepen F, Spethmann S, Kneitz R, Mossakowski A, Hahn K. Patient journey with Charcot-Marie-Tooth Disease - A German patient survey study. Orphanet J Rare Dis. 2026 Feb 3;21(1):84. doi: 10.1186/s13023-026-04236-2. PMID: 41634720; PMCID: PMC12958679.

Further readings:

- De Grado A, Serio M, Saveri P, Pisciotta C, Pareyson D. Charcot-Marie-Tooth disease: a review of clinical developments and its management - What's new in 2025? Expert Rev Neurother. 2025 Apr;25(4):427-442.
- McCray BA, Fridman V. Clinical Outcome Assessments and Biomarkers in Charcot-Marie-Tooth Disease. Neurology. 2024 Dec 24;103(12):e210120.
- Rossor AM, Haddad S, Reilly MM. The evolving spectrum of complex inherited neuropathies. Curr Opin Neurol. 2024 Oct 1;37(5):427-444.
- Stavrou M, Kleopa KA. Gene therapies for CMT neuropathies: from the bench to the clinic. Curr Opin Neurol. 2024 Oct 1;37(5):445-454.

- Parmar JM, Laing NG, Kennerson ML, Ravenscroft G. Genetics of inherited peripheral neuropathies and the next frontier: looking backwards to progress forwards. J Neurol Neurosurg Psychiatry. 2024 Oct 16;95(11):992-1001.
- Bolino A, D'Antonio M. Recent advances in the treatment of Charcot-Marie- Tooth neuropathies. J Peripher Nerv Syst. 2023 Jun;28(2):134-149.