Project 101232916 - EUCMTSC

Deliverable 1.4.

Event Report

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Key-words: 2nd European ECMT Specialists Conference, inherited neuromuscular diseases, CMT, dissemination, reference materials, webinars, livestream, press releases, reporting, video-takes, interviews with scientists, pharmaceutical industry, YouTube, patient readiness for partnership, patients as partners, Charcot-Marie-Tooth, gathering stakeholders to progress research

The 2nd European CMT Specialists Conference (EUCMTSC)

was held in Antwerp October 23 to 25, 2025. More than 130 participants from European Countries, the United States of Amerika, Israel, Brazil and South Korea, came together to present research achievements and to discuss and develop new strategies to improve the efficacy of the European health care system(s) for rare diseases and for CMT, in particular, in conformity with the objectives set out in EU Regulation 2021/522. Much progress has been made in CMT-research during the last decades. Scientists, physicians and other healthcare providers meet regularly in congresses such as the annual PNS meetings, workshops are organized, and many international groups of researchers work hard on promising projects. And yet, although the disease has been known since the nineteenth century, no disease-modifying therapies have been developed so far. Patients even get no or very late diagnosis – a diagnostic odyssey is typical for CMT – and patients increasingly feel hopeless and left behind, while their disability progresses slowly but inexorably towards the wheelchair and worse.

I. Objectives of the Conference

The Antwerp Conference was understood as a new impetus, based upon an innovative partnership approach, towards a cure for CMT. Its general aims were described in the EU4Health Grant Proposal as follows:

> *The thematic objective is the identification of shared, system-level roadblocks and opportunities to improve clinical care and accelerate biomedical research for rare inherited neuromuscular diseases (iNMDs) within the EU-health space. As the ERDERA program demonstrates, action on rare diseases remains a priority objective of EU health policies. The conference will create an urgently needed forum for EU-wide strategic coordination to complement the existing portfolio of national and international conferences dedicated to specific scientific, medical, or patient communities for iNMDs. To focus our discussion without sacrificing our ambition to foster the development of more general solutions, we will use Charcot-Marie-Tooth (CMT) disease as archetypical model for new initiatives within the iNMD space.*

The initiative to organize the Conference was based upon the observation, that the CMT biomedical research ecosystem faces several key roadblocks. Effective research and the development of efficient treatment methods often encounter difficulties due to…

1. *A lack of public awareness, but also a lack of clinical awareness and training needed to recognize the specific symptoms of CMT;*
2. *The fact that, despite significant progress, much of the genetic landscape of CMT remains to be mapped out, and even the significance of variants in known disease genes is often difficult to determine;*
3. *Our still incomplete understanding of the pathomechanisms underpinning CMT and related disorders;*
4. *The lack of sufficiently sensitive clinical outcome assessments (COAs) to feasibly power clinical trials with the result that even where promising therapeutic avenues emerge, clinical trials for many CMT subtypes are hampered.*

All this adds specific economic deterrents for industry to pursue drug development for CMT. Because they are rare, research in iNMD's and CMT, in particular, suffers from a lack of public support and a lack of investment; however, all of these do have a cost: a German study (2019) estimated the total annual cost of illness at €21.400 per patient, this coming close to €500M across the EU. A more comprehensive study on this socio-economic aspect is part of the work program undertaken in Antwerp.

Building on this, the ECMTF 2025 conference addressed two goals: (A) to improve research pipelines for earlier diagnosis and the development of pathomechanism-based treatment of CMT and related diseases, and (B) to raise awareness for this rare disease, define clinical outcomes, and get ready for clinical trials.

Our work strives to respond to clearly defined specific unmet needs in the present European health care systems specifically regarding rare diseases like inherited neuromuscular diseases (iNMD), and opportunities for rapid remedial action. As these diseases are rare, they…

- …receive less dedicated attention in medical training, which makes it more difficult to recognize them in daily practice. Ten years of diagnostic odyssey is the average time to diagnosis, which is unacceptable for a disease like CMT with an assumed prevalence of 1:2500. – Accordingly

  Objective 1 aimed at better understanding inherited neuromuscular diseases and CMT in

its various forms, depict the symptoms, discuss methods for assessing prevalence and present some seminal results of research on diagnosis and treatment, including outcome assessment of therapies and drugs, as a basis for targeted integration of CMT into the medical training programs, for raising awareness among doctors and in the general public and ensuring rapid diagnosis.

⇨ As a result of the discussions Deliverables 2.1.& 2.2. **"Medical training program CMT – recommendations and outline for online seminars"** were submitted.

- …are financially less attractive for clinics and medical centers to specialize in CMT and related neurodegenerative and neuromuscular disorders. In smaller, non-academic centers, resources including staff and equipment would rather be allocated to units dedicated to common diseases such as stroke, multiple sclerosis, or Parkinson's disease, which is also based on established refunding pipelines. It is, notwithstanding, an important mission to provide efficient health care for all, including patients with rare diseases, which should be based upon profound scientific knowledge, research and experience with a wide range of patients. Since specialized centers for iNMDs are not comprehensively distributed, patients need to travel long distances, limited by their disease-related immobility. Therefore:

  Objective 2 was to present and discuss new forms of digital consultation and telemedicine allowing patients to meet a specialist from wherever they live. This will allow their local doctors to receive instructions on how to provide the correct treatment on site and permit the specialized centers to collect the relevant data as needed for (AI-based) research and the development of a cure.

  ⇨ As a result of the discussions, with Deliverable 6.1. an **"Outline for a digital care strategy for CMT across Europe and beyond"** has been submitted.

- …are not in the focus of pharmaceutical industries, for a profitable market for new drugs may well be limited, even if discoveries would allow their development. Therefore, scientists or clinicians, even if they develop an interest in doing research in the field, cannot find the resources needed for intensive and promising research. Against this background

  Objective 3 was to include scientists and representatives of the relevant companies as industrial partners in (the discussion of) research initiatives and so to pave the way to cooperative projects with a realistic potential for results that pay off the investment.

  ⇨ Accordingly, a **"Model multistakeholder joint research project"** has been developed during the preparation – and discussed and finalized at the Antwerp Conference, and submitted as Deliverable 3.3.& 4.3.

- ….face a special hurdle to effective research since scientists and clinicians who embark on a rare disease have not only difficulties in meeting patients and collecting the data needed for their research, but they also have no access to a critical mass of health data as needed for a meaningful analysis and using AI. Despite previous efforts, GDPR and competitive incentives that permeate the research ecosystem remain major barriers for effective data sharing at all levels. To remedy this situation

  Objective 4 was to encourage incumbents, including researchers, their institutions, as well as patient advocacy groups to develop paths to feasible and GDPR compliant, pan-EU, and interoperable data sharing in line with Article 4 (f) of EU Regulation 2021/522, by identifying key pain points as well as draft solutions to mitigate them and thus facilitate the use of AI in diagnostics.

  ⇨ In this vein, an **"Outline for a data-sharing framework in conformity with GDPR and EHDS, and easily accessible for researchers"** has been submitted as Deliverable 3.1.

- … are not sufficiently known among patients and their caretakers to realize opportunities for positively influencing their illness. CMT patients often feel lie victims and treated as objects of medical care. As a result, they remain passive and are no more than recipients of services. In the best case, patients should actively take care of their own fate and take it as their personal goal to work together with therapists, doctors and researchers to keep their health condition as good as possible. Patients and their families are discouraged and depressed when, if at all they find a specialist and get a diagnosis and find a specialist, they are informed that there is no cure for CMT. Too often, they refrain from doing physical training, do not regularly visit their doctor

to receive advice nor monitor their natural history and are even reluctant to participate in clinical trials for new drugs as needed for progress in research and development of a cure. In this sense

Objective 5 was not only to raise public and, therefore, patients' awareness of iNMDs and of CMT in particular, but also to promote a completely different, positive attitude of patients, including consent to use their data and donations. We expect that a self-conception and mobilization of "patient as partners" would considerably accelerate the research process towards the development of a cure. The motto is: "patients as partners", and one of the objectives of the conference is to elaborate on this concept as well as on strategies to promote it among the patient communities.

⇨ To this effect, an outline on **"Cooperative Research & Development for a Cure of CMT - 'patients as partners'"** was discussed and elaborated at the Conference and submitted as Deliverable 6.2.

The innovative elements we strived to further develop at this conference were namely:

- The "patients as partners"-approach (mobilization of the patients), to partner research initiatives, clinical treatment, studies and clinical trials for new drug development.
- A digital communication system (telemedicine) to bridge the distance between patients / local physicians and the specialized centers needed to adequately treat the rare diseases at stake.
- A patient-owned or -driven health data management system within the framework of the EDHS, facilitating research and the use of AI in diagnostics and outcome assessment.
- A multi-stakeholder approach for boosting cooperative research processes with interdisciplinary research teams including industrial partners and organizations active in health policies.

Thus, the focus of the conference was practical, striving to fill remaining gaps in the CMT research landscape. We brought together the relevant stakeholders (scientists, clinicians, patients, industry, etc.) to create synergies and develop new scientific approaches, and discuss ways to introduce new technologies including AI (in compliance with the European AI Act) in the research process. We decided for ECRA to act as an incubator of joint research projects and mentoring grant-applications, for training next-generation scientists, and for organizing international scientific cooperation. We discussed ways towards a global health data storage and exchange system. ECRA was confirmed as the body responsible for implementing the decisions of the Conference and so to ensure the sustainability and continuation of the work undertaken at the conference, Europe-wide and beyond.

II. The Preparatory Phase

To organize the 2nd European CMT Specialists Conference was already decided at the 1st EuCMTSC in Paris, 9-10 June 2023, in parallel with the decision to create the European CMT Research Association (ECRA). A special "ECRA-taskforce" was established to implement these decisions. ECRA was registered as a charity association September 17, 2024. Together with ECMTF and the University of Antwerp ECRA was part of the consortium created to organize the Antwerp Conference. With the concept of the Conference ready by October 2024, the consortium decided to submit a grant proposal following a call under the EU4Health program and submitted it in January 2025. So, it successfully did – what made the project possible. The preparation process, basically, consisted of 8 steps:

1. A **Conference Website** was created to make publicly available all relevant information on and materials for the Conference (https://www.uantwerpen.be/en/conferences/2nd-european-cmt-specialist-conference/). This website still gives access to the program and to

materials for preparation, practical information and the outcomes of the conference, including videos, a photo gallery, and diverse reports.

2. The **draft program** was finalized and communicated to all potentially interested researchers, clinicians and other health professionals, patient organizations and potential industrial partners, with a "save the date" and the announcement that a "call for abstracts" would be issued in early summer for presentations, posters and joint projects to be discussed at the Conference.

3. A **dissemination strategy** was established and, accordingly, a first press release was distributed to get the public aware of the Conference and its objectives.

4. The organizers aimed for a high scientific standard and discussion of truly new approaches in research. To this end, a **call for abstracts** was issued for presentations and posters on key topics: the fundamentals and many faces of CMT, diagnosis, therapeutic approaches, data management, outcome measurement and clinical studies. Awards for the best presentations and posters were announced. This call resulted in many submissions, from which 21 presentations and 32 posters were selected – they became the basis of the final program of the Conference. The abstract book and the names of the award winners for the best presentations and posters are publicly available on the Conference website.

5. Diverse **reference materials** have been produced and published at the Conference website allowing participants and other interested people to inform themselves and prepare for the Conference. Among these materials, the following reading lists and lists of relevant activities have been published on the Conference website:

- Therapeutic Advances for CMT WP2 (G Fernandez)
- Socioeconomic impact of CMT, WP2 (T. Stojkovic)
- Data Management and Use of AI WP3 (W. Pernice)
- CMT Genetic and other Therapeutic Approaches WP4 (K. Kleopa)
- Outcome measurement and clinical trials WP5 (D. Pareyson)
- Running and Planned clinical trials WP5 (T. Vangansewinkel)

6. To adequately prepare the discussion of the role of patients in CMT-research a survey on **"Patient Readiness for Partnership in Research on inherited Neuromuscular Diseases (iNMD)"** was conducted among patient organizations; the result seems to be that patients are willing to engage and participate in research, but there is a lack of awareness and information about forms and concrete opportunities to do it. The report is published on the Conference website.

7. The **(Pre-)Antwerp Conference Webinar Series** has been established and broadly advertised in social media and through the national member organizations of ECMTF, to allow the interested public to learn about the subject and understand the need for action, but also to present the outcome of the Conference. All the webinars are now published on the Conference website:

05th May 2025, with Filippo Genovese / Alexandre Hoyau / Ingolf Pernice:

Patients in action: Introducing the tasks and activities of the CMT patients' advocacy groups in Europe and their Federation (ECMTF) as model for patient engagement and mobilizing patients to be partners in research

30th June 2025, with Davide Pareyson (moderation Filippo Genovese):

CMT/HMSN – a challenge for scientists and patients: The most critical symptoms, what are researchers doing to find a cure? How to live with CMT, hope and disappointments? How does it affect social life?

23th September, with Jonathan de Winter / Alexandre Hoyau (moderation Ingolf Pernice):

News from the PNS Congress Edinburgh, the scientists' perspective and the patients' perspective. New research findings presented and discussed at the conference, new questions posed. What do we learn from Edinburgh?

14th November 2025, with Vincent Timmerman & Ingolf Pernice (moderation Maike Dohrn):

Towards a cure for CMT? Takeaways from the Antwerp Conference: Highlights from research. What are the promises, what was missing, what should be the next steps?

8. The **CMT Awareness Campaign 2025** was lead from spring to October 2025 and included numerous posts and visuals about the Antwerp Conference. It was spread on social media in diverse European languages and had a considerable impact.

III. The Conference

The University of Antwerp hosted the Conference in its prestigious **Hof van Liere Conference Center** in the center of the city of Antwerp. A friendly, well-furnished and technically well-equipped conference hall with inviting side-spaces for coffee-breaks and the exhibition of the posters provided the guests with a welcoming venue for intense work and relaxed networking. This allowed participants to tackle the problems presented and grow together step by step into a new scientific community in an excellent atmosphere. The demanding program including the abstract book is available at the Conference Website, here. Many of the amazing introductions and presentations have been live-streamed; together with a special overview ("the best of…"), the video-interviews and the webinars around are published in the YouTube playlist dedicated to the Conference.

1. Opening Ceremony

The **Opening Ceremony** was started with a word of welcome by **Vincent Timmerman**, one of the leading researchers in CMT, elected president of ECRA and host of the Conference to all participants, including those coming from overseas. After a brief excursion to the origins – the discoverers of the disease: Jean-Martin Charcot, Pierre Marie, and Howard Henry Tooth –, a few words on the CMT research history and of the background of the Antwerp Conference in particular, he highlighted the aims and objectives of the event as part of a long-term strategy towards a cure of many forms of CMT. His intervention can be followed here.

This session provided an insight into the subject matter of the conference from the various perspectives: European health politics, science management, clinical diagnostics, industrial drug development, and patients as partners.

It was felt as a particular honor and appreciation of our initiative that the EU Commissioner for Health and Animal Welfare, **Olivér Várhelyi,** to begin with, sent us a video-message on

the “Highlights and future of EU Health Policies and Rare Diseases”. It was most encouraging to hear that European politicians are by no means losing sight of the specific problems associated with rare diseases, including CMT.

The Commissioner first referred to the important role the European Research Networks (ERN) already play – he qualified this as a true success story; and he emphasized the determination of the Commission to further develop them under the next multiannual financial framework within the window dedicated primarily for health and biotech under the European Competitiveness Fund. He emphasized the crucial role of research in the broader area of rare diseases – research that, in his view, opens doors to discoveries that change all of medicine. Pointing also to some other initiatives of European health policies aiming at improving outcomes for people living with rare diseases he concluded that this “needs all of us working together: patients, doctors, scientists, pharmaceutical researchers and policymakers. The EU will keep working with you to turn research and cooperation into real treatment and better lives”.

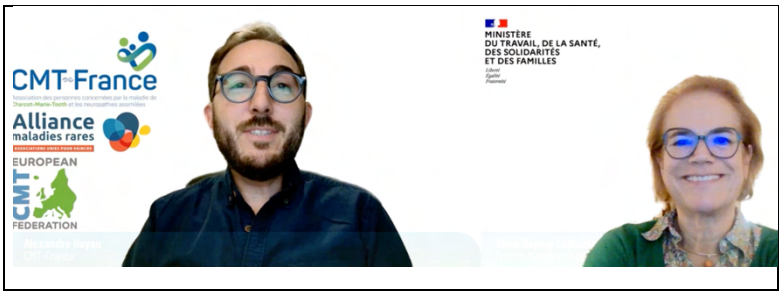
This positive assessment was clearly shared by **Davide Pareyson (Italy)** and **Kleopas Kleopa (Cyprus)** who explained more deeply the role of and opportunities for cooperative research that the ERN Euro-NMD offers. Davide Pareyson mentioned in particular the ERN Registry that is planned to be used for collecting ultrarare cases of CMT in view of future therapies. Kleopas Kleopa added that this Registry can also be used by ECRA for collecting rare CMT cases throughout Europe – it is the only existing way to do this. Another important example of research cooperation under the Euro-NMD is the new Inter-ERN group on gene therapies, that already offers a series of webinars open to the public, as well as a survey about gene therapy availability and access across Europe. Other initiatives within this ERN were finally mentioned such as the Clinical Patient Management System, open to all centers who want to submit cases, a task-force for transition, and the “patient journey” – a patient-led project in ERN, collecting experience of living with the disease from the patient perspective. The conclusion was that close cooperation of ECRA with the ERN would be of great value for both sides with a view to progress research in CMT. The same was true for the European Neuromuscular Center (ENMC). Given the aims of the ENMC, the easy application process and the opportunities it offers particularly for next generation researchers, the speakers particularly invited the audience to submit applications regarding CMT in the near future – no applications have been received in the field of CMT during the last nine years. This urgent appeal clearly fell on receptive ears among the group.

Tanja Stojkovic (France) explained, from the clinical perspective, the “Charcot-Marie-Tooth diseases and its mimics: the diagnostic challenge”. She gave an overview of the many variants of CMT and its “mimics” and presented the practical issues clinicians are facing at the stage of diagnosis. She described a series of recent cases

where the diagnosis revealed to be more than complicated. Symptoms sometimes suggest a diagnosis other than CMT; only with a very precise analysis of all circumstances was it possible to distinguish it from other conditions.

Evan Bailey, representing the biopharmaceutical company Applied Therapeutics, gave a promising account of the famous SORD trial that could become the first drug approved by the FDA and EMA for a specific type of CMT. Yet, he also pointed to the particular difficulties of assessing the long-term efficacy of a drug for a rare disease like CMT that progresses slowly over years. A first breakthrough for a disease-modifying drug would give the research activities in the area important new dynamics and support. So, the best wishes of the audience were given to Applied Therapeutics, the "industry-partner" that has already joined ECRA.

Not many policymakers had accepted our invitation to actively participate to the conference. Yet, it was a great pleasure for us to play a video-interview of the president of CMT-France, **Alexander Hoyau**, with **Anne-Sophie Lapointe**, policymaker from the national level and responsible for rare diseases policy at the French ministry of health. They talked about the new "Joint Action for Rare Diseases Integration of ERN's into National Healthcare Systems" (JARDIN), that she is pushing ahead for France – and beyond.



France is the co-leader of the JARDIN work package 8 on data management, and Anne-Sophie Lapointe explained the urgent need of better information about the natural history of patients with rare diseases and ultra-rare diseases. There is a lack of relevant data of rare diseases; thus, common registries would help to better understand them and to find participants to clinical trials for new drugs. The initiative of joining the efforts of the ERN's in this area and of connecting the so far isolated silos of data in clinics and research centers, she explained, is a priority of JARDIN. She emphasized that the patients are the center of this action, since it is about their data. CMT patients, like other patients affected by rare diseases, thus, are called to make their data available not only for drug development and clinical trials but also for the assessment, over longer time periods, of the effects of any (new) treatment.

The patients' perspective was taken up by **Ingolf Pernice**, coordinator of the Conference, vice-president of ECMTF founding president of ECRA and CMT patient himself. In his very personal statement he not only gave some insight in the challenges CMT presents progressively in a patients' life – and the socioeconomic costs it involves for the society, he also listed the diverse ways of how patients can contribute to facilitating and accelerating the research efforts of the relatively limited group of scientists and clinicians active in the field of CMT. His very positive experience with the patients' engagement, "as partners" of the

health professionals in favor of a structured multi-stakeholder cooperation at eye level, was aimed to mobilize other patients to become actively involved, in whatever form, of the CMT research process.

2. Plenary Sessions

Four **Plenary Sessions**, the first dedicated to basic sciences, the others dealing with diagnostics & genetics of CMT, with therapeutic approaches for CMT, and with clinical trials, data sharing and outcome measurement**,** have been combined with a **"fishbowl"-idea workshop** on joint projects and initiatives, and an **Open Session** for the discussion of new approaches of physiotherapy, digital care and the concept of "patients as partners" in CMT research, determined the scientific part of the conference. The presentations are summarized in the abstract book available together with the program at the Conference website. Here can also be found the YouTube playlist with several of the introductions and presentations.

a. Basic sciences and the many faces of CMT

The introduction given by Tanya Stojkovic at the opening session had already set the stage for the first plenary session. Six fascinating presentations showed not only a promising new method to do more effective research in CMT and better understand the mechanism of CMT in general, but also specific findings on CMT and the relationship with gene mutations causing other rare diseases.

Bieke Bekaert started the discussion with a presentation of an alternative method of studying myelination and neuron-muscle interactions: instead of animal models – which often fail to translate into therapies, her team creates hybrid models by fusing induced pluripotent stem cells (iPSC)-derived motor neuron spheres with immortalized muscle spheres. **Stijn in 't Groen** too uses this alternative approach for studying the impact of certain gene mutations on the neuromuscular junction. The method seems to be a major step towards more efficient research; it not only saves lives of animals but also time and costs of research in laboratory work and promises to considerably accelerate the study of the mechanisms causing CMT – and many other neuromuscular diseases. A comment in the audience referred to similar work of another lab and suggested joining efforts in a cooperation to be established.

Other presentations reported of more specific disease-related works and findings: **Francesc Palau** gave an account of the finding of his team that biallelic variants in the DARS2 gene can cause isolated axonal CMT with or without central nervous system involvement. - **Koen Kuipers** reported on his finding that inhibiting ATP-binding cassette transporter 1 (ABCA1), a membrane co-transporter involved in cholesterol and phospholipid efflux, restores key Schwann cell functions and represents a promising therapeutic avenue for functional recovery in CMT1A.- **Barbara Tedesco** presented her work on frameshift mutations in the heat shock protein B8 (HSPB8) causing novel players in HSPB8 pathology. - The power of long-read sequencing was shown by **Ilaria Quartesan**: She found that that gene–pseudogene inversions may represent largely overlooked pathogenic SVs in Mendelian disease when only short-read sequencing is used. Their systematic detection through long-read technologies, she reported, had the potential to improve diagnostic yield and inform future clinical decision-making.

b. Diagnostics and Genetics of CMT

With an impressive keynote on the contribution of sensors, robots and AI in the evaluation and treatment of inherited neuropathies **Angelo Schenone** introduced the second session. While telemedicine permits regular cost-effective monitoring of the utterly results of a treatment, in privacy and avoiding burdensome traveling, he sees AI as the glue binding together all the technical devices including sensors and robots. Robots can, as he explains, assist rehabilitation for neuromuscular diseases, though there is no scientific evidence yet for their utility – extensive clinical trials would be needed. Sensors, like the GAITrite system, have the potential for objective gait assessment and can give important information both on the process of the disease and on the outcome of therapeutic interventions. Similar findings were made with a Hand Test System (HTS). Robot-assisted therapy and rehabilitation, finally, would become increasingly important as a complementary method of treatment.

Four challenging presentations followed in this session, starting with **Gorka Fernandez-Eulate** who found six adult patients from five families with biallelic PIGB variants that are a cause of childhood-onset, motor-predominant neuropathy with conduction blocks and neuromyotonia. This suggested that PIGB-related peripheral neuropathy could represent a novel cause of inherited paranodopathy. - **Ayse Candayan** reported advances of genetic diagnostics in CMT and benefits of the long-read sequencing (LRS). In a study of 35 individuals from 14 families so far without a diagnosis, her team achieved a "28% diagnostic uplift through a combination of targeted and gene-agnostic approaches, providing long-awaited answers for families who had previously reached a diagnostic dead end". This is another testimony of positive experience with the power of LRS to improve the diagnostic yield for CMT, and, as she points out, it can become a first-tier test in CMT genetic diagnosis only if "we share our experiences, tools and data openly". - An interesting attempt to use AI to better assess misdiagnosis in the field of CMT, e.g. regarding CIDP, was presented by **Pedro José Tomaselli** from Brazil. Though the performance in his study was up to 87%, he concluded that the model may help neurologists in general, but not CMT specialists. - The talk of **Liedewei Van de Vondel** brought us back to another experience with LRS. Having combined several LRS technologies, her findings establish the 5' UTR of TBC1D7 as a novel disease locus and add to the disease-specificity of 5' UTR CCG expansions causing OPDM.

c. Therapeutic approaches to CMT neuropathies

A comprehensive overview given by **Kleopas Kleopa** of "the current status of therapeutics development for CMT neuropathies" introduced the discussions of the third session. Though time constraints forced him to be rather selective, his account shows that amazing work is being done, and considerable progress has been made promising first achievements towards a cure for one or the other type of CMT in the foreseeable future. Among the five stages of development of therapies only a few have reached the stage of clinical trials, none could achieve the regulatory approval yet. A rough distinction between pharmacological approaches and gene therapies allows us to get some order in the complex field. For the

first group, the most advanced development is the application of govorestat on CMT-SORD to reduce toxic sorbitol levels, followed by the specific target of using oral L-Serine to reduce toxic deoxysphingolipids levels in HSN1. A more general application has the NMD670 trial with the CIC-1 muscle chloride channel inhibitor to enhance the neuromuscular function; it is advanced close to the clinical trial, phase 3. Several other developments are still in the pre-clinical stage, but promising to shortly pass on to clinical trials: SARM 1 as the primary regulator of axon auto-destruction; histone deacetylase 6 (HDAC6) inhibition; the AGT-100216 HDAC6 inhibitor, already in phase 1trial; CIC-1 inhibition to treat CMT neuropathies; inhibition of TRPV4-specific antagonist GSK219; and different approaches to correct tRNA synthetase-associated peripheral neuropathies. In part even more advanced and close to translation and approval are certain disease-specific (axonal, CMT2, and demyelinating, CMT1/4) and non-specific approaches in CMT gene therapy. Whether it is a gene-replacement or gene-editing approach, gene silencing or CRISPR/Cas9, there is an amazing amount of advanced work with a considerable potential to come to translation soon.

Seven fascinating presentations rounded off the picture painted of the exciting developments in CMT therapeutics. It started with the account by **Nathalie Bernard-Marissal** of her study on CMT2A, developing and testing two novel therapeutic strategies aimed at restoring defective organelle contacts and associated pathways previously detected in CMT2A. The gene therapy approach using iPSC-derived motor neurons from CMT2A patients involved neuron-specific overexpression of wild-type MFN2, as well as a modified MFN variant designed to compensate for mutated MFN2. In addition, a pharmacological approach using IFB-088, an enhancer of the integrated stress response, was tested. As a result, both methods effectively restore ER-mitochondria interactions and improve mitochondrial function, resulting in reduced axonal degeneration. - **Nicolay Zhukovsky** reported a promising application of Alpha-1 Antitrypsin in a mouse model of CMT1A. With a two-weeks test only he found that AAT-treated mice exhibited marked improvements in neuromuscular strength and coordination compared to untreated controls, encouraging further investigation of AAT as a therapeutic strategy for CMT1A and potentially other neuropathies. - **Lara Cantarero** in her group had developed a new family of HDAC6 inhibitors that cross the blood-brain barrier. One of them, QTX153 was now tested in a Gdap1-/- mouse model, GDAP1- mutations being a leading cause of axonal CMT in Spain. The pre-clinical trials led, as she reported, to significant improvements in motor function of the mice. Further work on HDAC6-targeted therapies for GDAP1-related CMT, thus, is obvious. - **Alberto Raoss** presented the work of his team applying gene-editing technology to control PMP22 protein levels. The approach was to modulate the translational efficiency of the PMP22 mRNA by introducing targeted point mutations into the Kozak sequence of the PMP22 gene to decrease its codon recognition ability. Having achieved editing efficiencies above 30% for each variant the team will now validate the approach in patient-derived induced pluripotent stem cells (iPSCs) differentiated to Schwann cell precursors and hopes to so “paving the way for a ‚one-shot‘ gene therapy treatment” of CMT1A. - Another hopeful approach was presented by **Kim Hyeongseop** from South Korea, using EN001, an allogeneic WJ-MSC therapy developed by ENCell Corp, that was first tested in two single-dose first-in-human studies in South Korea: one for CMT1A (NCT05333406) and another for CMT1E (NCT06218134). Both patients with CMT1A and CMT1E showed reductions in CMTNSv2 after a single administration of EN001, indicating clinical

improvement. So, broader clinical trials, he said, are "required to confirm safety and efficacy of EN001". - **Natalia Dominik** reported her team's findings revealing ARHGAP19 loss-of-function as a novel driver of inherited neuropathy and supporting integrated Drosophila and cell-based studies to enable drug repurposing in CMT. - With her account of the more rehabilitation-oriented approach **Antonella Vitale** rounded off this session. Her study is looking at the structural involvement of the plantar fascia, a key element in foot biomechanics and stability. Her team explores the clinical relevance of plantar fascia alterations in CMT through non-invasive ultrasound imaging, and their correlation with functional outcomes, highlighting a potential new avenue for early, targeted rehabilitation. The study suggests that plantar fascia changes, detectable via fast, non-invasive ultrasound, may serve as early markers of functional decline in CMT and so could guide personalized physiotherapy and orthotic strategies as part of a patient-centered multidisciplinary approach for treating CMT.

d. Fishbowl "Idea workshops": Joint Projects and Initiatives

Two amazing projects have been presented in this idea workshop, the *CureCMT Doctoral Training Network* on "gene-therapies for rare CMT neuropathies: from pre-clinical development to clinical trial readiness" initiated by **Kleopas Kleopa**, and *the European Patient Journey in CMT*, initiated by Helena Pernice. The project idea for *CureCMT* already emerged from the Paris Conference. It is a truly multi-stakeholder joint project combining a multi-disciplinary doctoral training program with the topical challenge of developing effective treatments for several subtypes of CMT. It involves 15 leading scientists from 9 countries with a multi-disciplinary background, in close cooperation with 3 patient organizations and 3 industrial partners. The grant proposal being under review, this project was chosen to be our *model multistakeholder joint project* (see deliverable 3.3 &4.3). After presentation, three additional participants of the Conference spontaneously joined the group. The project is ready to start work. – The second joint research project presented at the conference proposes a "need-based digital approach towards early diagnosis and care in CMT". The group of nine mostly younger researchers, patient representatives, and some additional participants having spontaneously joined the group, envisages to know more about what the problems of the patients really are. So, **Helena Pernice** reported of a preliminary survey conducted with 270 patients in Germany as a first step. One of the results were that the average time a patient has to wait until receiving a proper diagnosis is 13,7 years, more than 50% having got at least a misdiagnosis first, almost 30% received wrong treatment, of which 56% have a permanent health damage and 27,5% having been wrongly hospitalized (see: Pernice, H.F., et al., Patient journey with Charcot-Marie-Tooth Disease – A German patient survey study. Orphanet J Rare Dis (2026). At this very early stage, it was suggested by the audience to organize an ENMC workshop to elaborate a European-wide joint project. The idea to combine this with a study on the costs of CMT received strong support.

e. Clinical trials, data sharing and outcome measurement

Clinical trials, data sharing and outcome measures were an important theme throughout the conference. Session four provided a dedicated forum for this topic. Opening the session, **Wolfgang Pernice** presented "DANCER: A new collaborative tool for ultra-scalable patient-partnered tracking of disease state and progression in CMT". Seeking to address persistent challenges in the design of clinical trials, the DANCER platform is an advanced AI system designed to deliver an easy-to-use, yet rich and highly sensitive new paradigm for outcome assessment through simple video collection. - **Connor Maltby** from Ulysses Neuroscience emphasized the limitations of existing clinical and electrophysiological scales in monitoring diseases progression, namely subjectivity and insensitivity to slow progression as in the case of CMT. In search of a meaningful biomarker of disease severity in CMT1A he found that Acetylated α-tubulin is a downstream target of HDAC6 currently under investigation for the treatment of CMT, and thus serves as a novel and disease-relevant biomarker reflecting molecular pathology and clinical severity in CMT1A. – **Michael M. Shy** reported of a study of the clinical natural history and molecular impact of PMP22 variants in CMT2E with 50 patients from 35 families. Twenty-four presumed disease-causing PMP22 variants were identified, and very diverse symptoms and varying severity. – **Marion Masingue** reported a case of a 54-year-old woman with a pauci-symptomatic demyelinating sensorimotor neuropathy. With whole genome sequencing a homozygous COA8 mutation (c.476+1G>A) could be identified, confirmed by diffuse COX deficiency and significantly reduced complex IV activity on muscle biopsy. – The session was concluded by **Alessandro Bertini** with a fascinating report of a study on the genotype-phenotype-correlation in a large cohort with HSPB1-related neuropathy.

f. Round table on access to therapy for patients with rare diseases

The fifth Plenary Session was more political: the **Round Table** with **René Westhovens** with 14 years of experience as political advisor on rare diseases in the Belgian ministry of health, **Davide Pareyson** and **Maike Dohrn** for the researchers perspective, and **Alexandre Hoyau** (with an enlightening statement on the role of the patient advocacy groups) discussed the issues of "access to therapy for patients with a rare disease: from studies to approval, reimbursement and optimal use". Westhovens shared highlights and insights from his 40 years' experience as rheumatologist and his work in the field of regulatory aspects and reimbursement of drugs including for rare diseases, some of which were taken up in the round table, supplemented and discussed. Among the main takeaways the following key messages may be mentioned: (1) always take a positive perspective; (2) close cooperation between basic sciences and clinical science, but also with patients is key; (3) have and communicate a correct perception of the disease; (4) standardization of outcome measuring are beneficial to the patient; (5) formal quantitative evaluations and realistic predictions of costs help building trust with payers and governments (6) participation of, and shared decision-making with patients is fundamental for successful strategies; (7) health economic issues like information on the cost of the disease are crucial for decisions on issues like fast access to approved drugs; (8) education by specialized centers to general practitioners and

information about the disease to the public are important; (9) do not wait for an ultimate cure, but start treatment and proper care immediately - therapy by health professionals not only mitigates the symptoms and slows down the progression, but also improves the outcome of drugs; (10) establish a platform for the patients with standards of care – talk to the patients, council them, show pictures, and eventually have the patients ready for clinical trials; (11) consider the approval of therapies as a co-responsibility of all stakeholders involved; (12) when approved, the period when a drug comes to the market is very diverse in European countries – the better the disease and its gravity – and costs – are perceived, the shorter this period may be; (13) the approval of one first drug would rapidly pave the way towards the development of other drugs; (14) rethink the concept of patient; it is already a judgment against the affected person to be patient and suffer, follow advice etc., instead being the co-pilot of recovery.

g. Open session: Physiotherapy / digital care / patients as partners

Gita Ramdharry started the *open session* with an introduction into the "physical management of CMT: understanding the mechanisms of rehabilitation approaches while supporting people to live well". The question of how the primary disease-progress can be addressed, be interrupted or even be reversed one day by specific neuromuscular focused exercises is a relatively new research topic. Already existing studies based upon systematic review of randomized clinical trials show that strengthening exercises have a positive effect at least for proximal muscles. For distal muscles a fast trial with not too severely affected children showed that specific exercise over six months resulted in a 30% strength increase, though there was no increase of the muscles size; so, it might just be a neural change. Regarding skilled activities like gait, balance, hand dexterity, a study with 26 CMTA1 patients training for 3 months with stretching and "proprioceptive" exercise on treadmills showed improved walking speed and endurance, but also improved balance, "so doing something helps". Self-management in partnership with the patient had a significant effect size. Psychological support and motivation are key. Only ¼ of the patients asked continued the exercises after the end of the study, for those who did support by therapists was essential. There are guidelines on supported self-management, which translates the patient as partners approach in practice, and such a change of perception, based upon trust and reliance with the health care professionals promises to be a way towards an answer to the initial question.

Helena Pernice followed with a very practical proposal striving to manage access to specialized care to patients across long distance particularly in cases of CMT-related mobility issues: Digital care – challenges and opportunities for a CMT community "without borders". Digital care is presented as a solution for how to bring specialists, new research achievements and trials to the patients and how to bring patients to the specialists, other specialized health professionals and clinical trials. Telemedical consultations and examinations directly in the primary care physicians' practice, follow-up examinations, care, and treatments by the teleneurologists, and long-term follow-up via specific direction to specialized neurological practices in the area or via telemedicine are actually studied to tackle the problems. Not all, but many important examinations, like estimating disease severity from videos of gait, do work via the camera. Patients can relate to care via apps and devices, which saves time and allows history taking by patient-recordings. Shareable data can be

collected more easily for joint registries, with bigger cohorts, and participants for new studies can more easily be found. INC, JARDIN and the Registry Hub for Rare Neuromuscular diseases of the ERN Euro-NMD network were mentioned as examples to develop further so to eventually provide researchers with the data needed for their respective studies (see deliverable 6.1).

All this requires a more open and active attitude of the patients. So, the account given by **Katherine Forsey** of the CMTA Experience with "Patients as Partners in Research" gave an excellent insight of a very successful initiative by the American CMT Association, to mobilize the patients and establish a powerful registry. "Patient voice and patient participation", she says, "is what shapes the future of CMT research". Patients are eager to be updated with developments in research on CMT, while researchers often have no access to patients ready to participate in studies and trials. The "Patients as Partners in Research Platform" was created to empower patients and to have a trusted place to share research opportunities with the CMT patients. Meanwhile it is a powerful tool with global impact and already 8700 profiles 49 CMT subtypes represented and over 36 studies supported. Three examples of European projects funded by CMTA show an overwhelming readiness of patients to cooperate in research and development of therapies through the platform so established. The audience and CMT patients were invited to register, be informed on recent research achievements and actively participate in and support research on their own disease.

The last word being for those who are most concerned, **Alexander Leysen**, speaking for Spierziekten Vlaanderen, Belgium, explained the "objectives, work and visions of a patient organization". He explained the important tasks of patient organizations in education and providing trusted information, offering emotional support to patients, guiding patients through their healthcare systems, advocating for their needs in policy and research and fostering solidarity within the patients' community and as a part of society. Inclusion, awareness and equal rights are only three of the keywords used to describe the objectives pursued. And all this not only for the patients, but also for their families, friends and the social context they live in. Giving patients a voice also on medical decisions and research agendas is another task. Major challenges, in turn, include a lack of funding as well as administrative burdens, including those related to grant applications. The call-to-action points to three wishes: Take us seriously, accept patients' involvement, and "don't look at us as a waste of public money – we see it as investing in a society open for all people".

3. Poster Sessions – the Daniel Tanesse awards ceremony

32 amazing posters on recent findings and achievements, new methods, surveys and innovative projects have been presented in two poster sessions. This was an opportunity for all participants not only to mingle and network, but also to discuss new joint projects to be developed in the follow-up period.

The **best posters and the best presentations** were selected using an electronic process to ceremoniously award the Daniel Tanesse Prize. The President of the ECMTF and newly elected Vice-President of the ECRA, **Filippo Genovese**, presented the six winners congratulated them to their remarkable work. For the best posters the winners are (from left to right):

- Karen Libberecht
- Melanie van Brussel
- Alexia Kagiava (no photo)

The winners of the awards for the best oral presentations are

- Gorka Fernandez
- Koen Kuipers, price received by Ester Wolfs
- Bieke Bekaert

The entire audience gave these young talents a great and warm applause, with best wishes for their further studies – to the benefit of the CMT-patient community

4. Backstage interviews with key opinion leaders

In parallel to the sessions of the conference, six fascinating interviews were held with leading scientists, clinicians, patient representatives and speakers of our industrial partners:

- Multi-stakeholder joint research projects?
  - Guests: **Nathalie Bernard-Marissal & Kleopas Kleopa**
  - Topic: How basic scientists and clinicians can bridge the gap to create projects that move faster toward trials.
- Can drug development in CMT be profitable?
  - Guests: **Maike Dohrn & Evan Bailey**
  - Topic: A candid look at the economics of rare disease drugs and how industry views the CMT market.
- Genetics of CMT: The way ahead towards a cure?
  - Guests: **Lara Cantarero & Mary Reilly**
  - Topic: Whether finding more genes is still the priority, or if we should focus on treating the ones we already know.
- Roadblocks for drug development in CMT
  - Guests: **Filippo Genovese & René Westhovens**
  - Topic: The regulatory and reimbursement challenges that exist *after* a drug is proven to work scientifically.
- Patient readiness and recruitment for clinical trials
  - Guests: **Connor Maltby & Alexander Leysen**
  - Topic: How patient organizations prepare their communities to fill clinical trials quickly and effectively.
- Perspectives for young CMT researchers
  - Guests: **M. Drummond, M. Van Brussel & G. Fernandez**
  - Topic: The next generation of scientists discuss why they chose the CMT field and what excites them most.

5. Conclusions and the Way Ahead

The final highlight of the conference was the concluding session with the newly elected president of ECRA and host of the event: Vincent Timmerman. He was introduced by the chair of the session, **Mary Reilly**, with encouraging words about the great merits Professor Timmerman has earned over the past decades since he had discovered the first gene in CMT, with a warm recognition of the work of ECMTF to bring together the patient organizations from all over (geographical, above politics!) Europe with the patients getting active for finding a cure in the broadest sense and initiating ECRA to boost research to this end – and with thanks also to the organizers of the conference. **Vincent Timmerman**, the new president of ECRA, gave an overview of the impact and ambition of ECRA for a follow up of the conference, including communication, dissemination and visibility action on the ECRA website, reviews and reports in medical journals, social media, reports at relevant congresses (e.g. PNS) and many proposals for ENMC workshops. In the future work interoperable registers and access to the relevant data for researchers would be one priority, but also a dialogue with other rare diseases, e.g. within the framework of EFNA, to learn from each-other and act jointly where possible for awareness and recognition of CMT and other iNMD as relevant diseases: Dance together, with reference to the DANCER-project, scientists, clinicians, patients and, not to forget, policy-makers, this was his call to the grateful audience.

Standing ovations honored the extraordinary engagement and commitment of Vincent Timmerman and his team with ECRA to make a fresh start in our joint action on CMT and other iNMD's.

IV. Follow-up

For the follow-up of the conference and the implementation of the decisions taken the ECRA 5-year action plan is in the making and will be adopted early March 2026. So far, five activities and achievements deserve mention: dissemination activities, an evaluation of the conference, new projects emerging from the conference, the ECRA-website established and a comprehensive overview of CMT published in a leading scientific journal.

1. Dissemination activities

A flurry of spontaneous enthusiastic comments and reports on **social media** followed immediately after the conference ended, even before the post-event dissemination strategy could be rolled out. A **press release** has been published shortly after the closure of the Conference. A few days later, Filippo Genovese has published a **Comprehensive Report** of the 2nd European CMT Specialist Conference with links to the videos available of selected sessions and of the interviews held was published by the President of ECMTF under the title: "Uniting Science & Community", with the videos taken of selected sessions and presentations.

Nothing could better illustrate the focused yet friendly, collegial and sometimes enthusiastic atmosphere at the conference, including the gala dinner, than the short video 'The Best of' and the photo-gallery, both to be found on the conference website. Other publications and dissemination activities followed (see the dissemination report, Deliverable 1.6).

2. Evaluation of the conference by the participants

To assess the quality of the conference a survey has been conducted with a number of relevant questions regarding the significance, the innovative contents and the quality of the talks and presentations, the general management and the benefits of the conference for participants. The result was overwhelmingly positive, showing that nobody regretted having spent time participating, and a great majority wish to have more such conferences in the future. The **evaluation report** is published on the Conference website: Summary of the evaluation survey (Deliverable 1.7).

3**. New projects emerging from the conference**

Two new joint research projects were presented, discussed and welcomed for support by ECRA already in the "idea workshops" (supra III.2.d). Yet, the networking and discussions of posters and presentations gave also rise to further excellent ideas for new joint projects. At least six projects deserve mention here:

a. Data-sharing framework in conformity with GDPR and EHDS (deliverable 3.1)
b. AI in CMT – research, diagnostics, outcome assessment (deliverable 3.2)
c. Model multistakeholder joint research project (deliverable 3.3 / 4.3)
d. Need-based digital approach towards early diagnosis and care in CMT (supra III.2.d)
e. Digital Care strategy for CMT across Europe and beyond (deliverable 6.1)
f. Towards Rehabilitation Guidance for the Management of Adults Living with CMT (deliverable 4.1)

4. The ECRA Website

A Conference-website had been established by the University of Antwerp specifically for this event; it will not be maintained beyond a limited period yet. As the task of ensuring the implementation of the decisions taken at the Conference as well as the sustainability and further support and development of research on iNMD's and, in particular, CMT was entrusted to ECRA, a **special ECRA Website** was created with all the relevant materials from the Conference, and where all new steps and achievements in the field of CMT will be reported (www.ecra-np.org). The website will be further developed as a central instrument of information, communication and cooperation among scientists, clinicians, other health

professionals, patient organizations and industry partners, with the view of driving ahead the process of structured cooperative research and development in CMT.

5. Comprehensive overview of CMT published

In parallel to – and in connection with – the Conference, a group of conference participants together with other CMT specialists published an **outstanding scientific paper on CMT** in January 2026 in "Nature", a world-leading science journal. It reflects the current state of scientific knowledge and provides a comprehensive picture of the disease and how to deal with it: *Joshua Burns, Vincent Timmerman et al.*, Charcot-Marie-Tooth disease and related neuropathies, Nature Reviews Disease Primers (2026) 12:3. Given the considerable outreach of this publication it promises to be a great leap in the professional and public knowledge and awareness for the subject. In a summary titled "A Landmark 2026 Update: An Important Review on Charcot-Marie-Tooth", published on the ECMTF website, a recap written by **Filippo Genovese** in an easily understandable language, this "significant milestone for our community, offering a global consensus on the epidemiology, mechanisms, diagnosis, and management of CMT" has been made accessible to a broader public.

V. Conclusions

The 2nd European CMT Specialist Conference was far more than a three-day meeting; it was a strategic investment in building a resilient, collaborative, and patient-focused research ecosystem for a significant rare disease in Europe. The EU funding was instrumental in achieving all stated objectives, from executing a successful digital engagement campaign to launching a permanent research association in ECRA. The knowledge shared, partnerships formed, and infrastructure established during this event will have a lasting and meaningful impact on the CMT community for years to come.

The organizers and all participants of the conference herewith express their sincere acknowledgment for the generous support by the following institutions having made this event possible: