

welcome

Welcome to the latest TREAT-NMD newsletter. This week's edition features a report from our recent Governing Board meeting in Budapest plus details of some interesting upcoming meetings and two new Cochrane reviews, and sad news of the death of George Karpati on 6 February aged 74.

As always, we hope you enjoy the newsletter and look forward to hearing your comments - write to info@treat-nmd.eu with anything you'd like to say. Feel free to forward this message to anybody you think might find it of interest, or invite them to sign up to receive the newsletter by visiting our website. Back-issues of this newsletter can be found on our website at <http://www.treat-nmd.eu/patients/news/ezine-archive/>

Best wishes,

Katie, Volker, Hanns, Steve, Emma, Rachel and Sam: the Newcastle TREAT-NMD team

at a glance...

[28 Feb 2009 - 01 Mar 2009 First Asian conference on Duchenne muscular dystrophy \(DMD\)](#)

[26-27 Mar 2009 UK Neuromuscular Translational Research Conference](#)

[12-15 May 2009 The Nottingham Systematic Review Course 2009](#)

[21-23 May 2009 International conference in Ukraine: Recent standards in diagnosis, treatment and medical care for some rare neuromuscular diseases](#)

[01-03 Jun 2009 Update in Neuromuscular Disorders course in London](#)

[04-06 Jun 2009 TREAT-NMD workshop: clinical trial design in neuromuscular diseases](#)

[09-11 Jul 2009 "Therapeutic Targets in CMD", Emory University, Atlanta, Georgia](#)

[09-12 Sep 2009 IDMC-7](#)



TREAT-NMD Governing Board meeting in Budapest

The fourth meeting of the TREAT-NMD Governing Board took place in Budapest from 2-4 February. This meeting brought together representatives from all the network's partner organisations (with the exception of those snowbound in London!) and also included a meeting of its scientific advisory body (STAC: Scientific and Technological Advisory Council) who were present to receive an update on TREAT-NMD's activities in the past year and to advise the network on its future direction.



Establishing the Global Patient Registry has been one of the network's major achievements to date. The Global Registry has 12 national registries for DMD already running worldwide, with around 5000 patients already registered, plus another 8 under construction and several more in the planning stage. SMA numbers are slightly lower but reflect the same trend. The Global Database Oversight Committee is up and running, which means that researchers and pharmaceutical companies are able to come to us for data from the global database into which all the individual registries feed. A recent feasibility enquiry into DMD patients worldwide with specific mutations provided some exciting results that proved the tremendous utility of the registries as a tool for trial feasibility and recruitment, and a number of companies are approaching us for data and will hopefully recruit patients for trials through them in the coming period. It has also been very exciting to see the way the registries initiative has catalyzed support from patient advocacy groups as well as researchers and clinicians across the world.

Further to the success of our harmonized approach to the EMEA regarding outcome measures for SMA trials in 2008, a second meeting is planned for autumn 2009. This time the discussion will focus on the specific issues surrounding trials with antisense oligonucleotides in DMD. EMEA have expressed their willingness to work with the field on this kind of broader approach to guide future trial development in areas where no precedents have yet been set as this should substantially ease the process when individual therapies come under consideration for approval.

During the meeting it became increasingly clear that the separate "activities" going on within the network are all now linking together to form a coherent structure, and plans were also presented regarding the many opportunities for future application of the network's tools - the trial sites infrastructure, the patient registries, standards of care and other aspects of "trial readiness" developed over the past two years - to provide a "therapeutic platform" that will speed up trials and implement patient care. This strategy is expected to take substantial steps forward in the coming months.

TREAT-NMD has also supported several other research project applications. One of these, NMD-chip, has already received EU funding under the FP7 scheme, while a second project on biomarkers, BIO-NMD, is still under consideration. Researchers in Barcelona also were successful in obtaining funding in Spain for a research project on viral vectors which will link in with TREAT-NMD. All of these projects are excellent examples of the way TREAT-NMD, as an overarching "infrastructure", can provide the framework to support additional projects addressing a specific topic within the neuromuscular field.

The TREAT-NMD Project Ethics Council also met in Budapest and their animated discussion covered aspects such as the importance of increasing the "patient voice" in TREAT-NMD and specific questions raised by consortium members on issues such as the use of the same patient cohort for multiple phases of a trial. A meeting of the programme committee for the TREAT-NMD international conference taking place in Brussels in November also enabled substantial advances in the planning of this event, which promises to be a highlight of the neuromuscular calendar for 2009. Registration for the conference will open shortly so look out for it in a coming newsletter!

For a geographically dispersed network like TREAT-NMD, with partners across Europe and members and supporters all over the globe, the opportunity for face-to-face contact is often a rare event. When it does happen, it provides a valuable opportunity to move forward on joint activities and also reinforces

the real importance of the "networking" that is beginning to reshape research and care in the neuromuscular field.

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Death of leading neuromuscular expert George Karpati

Dr. George Karpati, one of the leading experts on the diagnosis and treatment of neuromuscular disorders, has died at the age of 74.



Born in Debrecen, Hungary, George was Professor of Neurology and Neurosurgery at McGill University, Montreal, and held the Izaak Walton Killam Chair in Neurology at the Montreal Neurological Institute and Hospital. He was a distinguished clinician scientist and the Coordinator of the Neuromuscular Group at the MNI for many years. George obtained his M.D. from Dalhousie University in 1960 and conducted his post-graduate training at the Montreal Neurological Institute and Hospital, the Henry Ford Hospital in Detroit, MI and the National Institutes of Health in Bethesda, MD.

George's greatest achievements were in Duchenne muscular dystrophy. He was the first to show the localization of dystrophin to the muscle fibre surface and to demonstrate a lack of dystrophin in the fibres of Duchenne patients. His research covered a broad range of basic and clinical studies on neuromuscular and neurological disorders, utilizing a broad spectrum of technologies including clinical science, histology, cytochemistry, molecular biology and genetics.

George's research over the years resulted in approximately 250 original research papers and review articles published in major respected biomedical journals and numerous invited lectures and visiting professorships. In addition, during the past four years, George edited or co-authored five major books pertaining to the neuromuscular field including the first modern text on neuromuscular diseases written in Hungarian.

Throughout his career he was honoured with many awards including the Order of Canada, the Order of Quebec (Knight), membership in the Royal Society of Canada as well as the Hungary's Academy of Sciences, a Lifetime Achievement Award in Neuromuscular Research and Clinics from the Muscular Dystrophy Association of Canada, and a Lifetime Achievement Award from the World Federation of Neurology. In 2005 he was elected to the Canadian Academy of Health Sciences and in 2006 he was awarded the Prix Wilder Penfield (Prix du Québec). He was awarded an Honorary Doctorate from the University of Debrecen in Hungary, his birthplace, and in 2008 was honoured with a Lifetime Achievement Award from the MNI.

George was known personally to a great number of TREAT-NMD colleagues, who would like to pass on their sincere condolences to his family.

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TREAT-NMD workshop on NMD clinical trial design 4-6 June 2009

One of the most common reasons for failed trials is poor protocol design. As neuromuscular disorders are very rare, clinical trials have to be multi-centre or even multinational to include enough patients. As a result, the study design for these trials is usually complex. Also, academic trials have come to face a changed regulatory environment following the implementation of the EU Clinical Trials Directive 2001/20/EC.



The aim of this workshop is to improve the efficiency of clinical trials in neuromuscular diseases by

- introducing future investigators to the fundamentals of effective clinical trial design by means of lectures
- developing study protocol drafts in small group sessions in conformance with ICH-GCP
- fostering contacts between investigators to facilitate later multinational cooperation through informal discussion sessions

This workshop is aimed at physicians specialising in neuromuscular diseases who are already involved in clinical trial work. One focus will be on study design in small numbers. Participants are asked to bring a draft study plan to provide the basis for writing a synopsis during the workshop.

For further information and to register for this course please download the [workshop flyer](#).

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Update in Neuromuscular Disorders, London, 1-3 June 2009

At the Clinical Neuroscience Centre Lecture Theatre,
National Hospital for Neurology and Neurosurgery,
33 Queen Square, London WC1N 3BG

Click [here](#) for provisional programme.

This course, now in its second year, is the result of the merging of two popular annual courses with an established international reputation:

1. the "Hammersmith Hospital update" on the latest research aspects, clinical and management advances related to childhood neuromuscular disorders, and
2. the "Institute of Neurology Neuromuscular short course", a stimulating update on adult inherited and acquired neuromuscular disorders

Course organisers;
Prof Francesco Muntoni, Dr Adnan Manzur, Dr Mary Reilly and Prof Mike Hanna

Topics to be covered include:

- Congenital Myopathies
- Spinal Muscular Atrophy
- Steroids and Duchenne Muscular Dystrophy
- Limb Girdle Muscular Dystrophies
- Duchenne Patients in adult practice
- Novel genetic therapies for Duchenne
- Muscular Dystrophy
- Charcot-Marie-Tooth Disease
- Metabolic Myopathies
- Channelopathies
- Inclusion Body Myositis
- CIDP and multifocal motor neuropathy
- Vasculitis
- Myasthenia Gravis – autoimmune and diagnostic
- Protocol for management of Myasthenia Gravis in 2009
- Animal models of Motor Neuron Disease
- Management of Motor Neuron Disease

Please contact Zoë Scott z.scott@ion.ucl.ac.uk or z.scott@ion.ucl.ac.uk for further details, and see

http://www.cnmd.ac.uk/index_courses for full programme when finalised

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New Cochrane reviews on SMA published

Drug treatment for spinal muscular atrophy type I

The review authors identified 1 small randomized controlled trial of riluzole involving 10 participants.

The review authors conclude:

'No drug treatment has been shown to have significant efficacy for SMA type I. Possible drug treatments for SMA type I should be sought and large randomized placebo controlled studies are needed to show the efficacy of drug treatment. A larger trial with riluzole is needed to evaluate to what extent this drug could be efficacious. Future trials should report possible side effects, especially the serious adverse events. The time from the beginning of treatment until death or full time ventilation should be the primary outcome measure. The (intensive) supportive care in each treatment arm should be the same. The change in motor function, daily functioning, and quality of life should also be considered as outcome measures. Developing a new functional rating scale or choosing an existing functional rating scale as a standard scale for all trials is recommended. Study investigators in multicenter trials should be well trained to reliably and consistently measure muscle strength by quantitative myometry and pulmonary function to avoid large variation in the measurements between and within the participating centres'.

A further randomized controlled trial of hydroxyurea is ongoing.

Bosboom WMJ, Vrancken AFJE, van den Berg LH, Wokke JHJ, Iannaccone ST. Drug treatment for spinal muscular atrophy type I. Cochrane Database of Systematic Reviews 2009, Issue 1.

<http://www.mrw.interscience.wiley.com/cochrane/clsystrev/articles/CD006281/frame.html>

Drug treatment for spinal muscular atrophy type II and III

The review authors identified four randomized controlled trials of treatments for spinal muscular atrophy type II and III. Treatments were creatine, phenylbutyrate, gabapentin and thyrotropin releasing hormone.

They concluded:



'Although some drugs looked promising in open or uncontrolled trials, the results of randomized placebo controlled trials have been disappointing. Thus, there is still no evidence of significant efficacy for any drug treatment for SMA type II or III. Potential drug treatments for SMA II and III should be sought and large randomized placebo-controlled studies are necessary to establish the efficacy of these therapies drugs. We would foremost recommend a trial with riluzole. Drug treatment in future trials should be given for an extended period of time and patient follow up should be sufficiently long (preferably at least one year for both treatment and follow up). Change in motor function, disability, muscle strength, pulmonary function and quality of life should all be assessed as outcome measures, and possible side effects, especially serious adverse events, should be clearly reported. Developing a new functional rating scale or choosing an existent functional rating scale as a standard scale for all trials is recommended. Also the time from the start of treatment until death or full-time ventilation should be evaluated. The (intensive) supportive care in each treatment arm should be the same. Study investigators in multicenter trials should be well trained to reliably and consistently measure muscle strength by quantitative myometry and pulmonary function to avoid large variation in the measurements between and within the participating centers'.

Two further randomized controlled trials have been completed but data were not yet available for assessment. Five randomized controlled trials are ongoing.

Bosboom WMJ, Vrancken AFJE, van den Berg LH, Wokke JHJ, Iannaccone ST. Drug treatment for spinal muscular atrophy types II and III. Cochrane Database of Systematic Reviews 2009, Issue 1

<http://www.mrw.interscience.wiley.com/cochrane/cdsysrev/articles/CD006282/frame.html>

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UK Myotonic Dystrophy Support Group Annual Meeting and Conference

The Myotonic Dystrophy Support Group is a UK charity supporting patients and families affected by Myotonic Dystrophy. Each year the group runs a national conference with invited speakers.

This year's conference will be held on Saturday 16th May 2009 at the Crowne Plaza, Marlow, Buckinghamshire.

Please contact the office on 0115 9875869 for more information or visit <http://www.mdsguk.org/conference.htm>



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