TREAT-NMD Partner Newsletter No. 16 and Club of Interest Newsletter No. 10

22nd June 2007

Welcome to the tenth newsletter for the TREAT-NMD Club of Interest. This week's edition features a report from the recent patient database curators meeting in Paris (section 3). Please also take a look at the FP7 Health call in section 4 and the Moleda summer school mentioned in section 5.

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.

Best wishes,

Katie, Volker, Stephen, Emma, Arron and Rachel – the TREAT-NMD coordination team

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Newsletter contents

1. About this newsletter

This is a weekly newsletter sent to all members of TREAT-NMD's "Club of Interest" worldwide. We are receiving new subscriptions all the time, so if you've missed the earlier editions of the newsletter and would like to catch up, please visit our newsletter archive online at http://www.treat-nmd.eu/news/newsletter/ where you will find all back-issues. If you have received this letter from a friend or colleague and would like to subscribe directly, please visit our website at http://www.treat-nmd.eu/ where you will find a subscription form at the bottom of the homepage. You can also use the same form if you no longer wish to receive this newsletter – just select the unsubscribe button.

2. Working with us

TREAT-NMD aims to be an inclusive rather than an exclusive network, and you do not have to be based in Europe or be a partner to be involved. International collaboration with experts from all over the world is already taking place, and new links are being developed.

If you are involved in any of TREAT-NMD's areas of interest and have something you'd like to say or a suggestion of where we could work together, we encourage you to get in touch by writing to us at info@treat-nmd.eu

3. TREAT-NMD news and reports

TREAT-NMD database curators meeting, 11 June 2007

Meeting report by Hanns Lochmüller (hanns.lochmueller@med.uni-muenchen.de)

On June 11 2007, the first TREAT-NMD workpackage 04.2 curator meeting took place at the Eurordis headquarters in Paris. The meeting was convened by Christophe Beroud (work package leader) and Hanns Lochmüller (activity leader), and attended by representatives of participating members (UNEW, MD-NET, FTELE, AFM, INSERM, NIEH) as well as guests from Switzerland and the US.

The aim of WP04.2 is to develop and manage supranational patient registries/databases for neuromuscular disorders, in particular Duchenne Muscular Dystrophy (DMD) and Spinal Muscular Atrophy (SMA). The curator meeting reviewed and compared already existing registries, agreed on the mandatory core set of data, discussed the legal and ethical framework, and developed a plan for implementation of the European registries on DMD and SMA.

The primary objective of the European TREAT-NMD registries on DMD and SMA is to assess feasibility and to aid planning and recruitment of clinical trials. Other secondary objectives may include studies of epidemiology, genotype-phenotype correlations, natural history, standards of care, etc. For SMA, national registries do not exist in Europe. For DMD, national registries exist in France, the UK, and the Czech Republic. These registries are not currently harmonized. They use different modes of data collection and updating, different levels of data protection and informed consent, and collect different sets of data (for an overview see www.treat-nmd.eu/biobanks). National curators for the TREAT-NMD registries on DMD and SMA will be located in Newcastle, Montpellier, Ferrara, Munich and Budapest. Already existing and new registries will be integrated and feed into the European meta-database. Collaborations have already been set up between TREAT-NMD, PPUK, the United Dystrophinopathy Project run from the University of Utah, and the Czech Parent Project.

A simple mandatory set of data was discussed and agreed on for SMA and DMD. This was aided by previous discussions on the TREAT-NMD website forum and by the 152nd ENMC workshop in Naarden. The mandatory data items that are to be uniformly collected by national registries for each DMD and SMA patient are as follows: personal and contact data of the patient, mutation, ambulation, steroid use and respiratory status.

National registries are encouraged to run optional modules such as assessment of standards of care and to coordinate this action with other TREAT-NMD activities.

The legal and ethical framework was explained by S Geismann (lawyer, Germany) and C Roy-Toole (barrister, UK). Patient registries are regulated by EU directive 95/46/EG on data protection, which has been implemented by national legislation in all member states and secures a very similar level of data protection in all countries within the EU. In general, personal data is protected, and there are fewer requirements for irreversibly anonymised data. The general principles are accuracy of data and minimisation of data. However, if the research (database) is expected to have a direct impact on patients, irreversible anonymisation is not appropriate, since it is necessary to retain some way of linking the data back to the individual patient (for example to notify them that they may be a suitable candidate for an upcoming clinical trial). This is in keeping with intended TREAT-NMD operations and demanded by participating patients and patient organizations. Accordingly, it was agreed on to use pseudonymised (encrypted) data and to implement informed consent procedures. Feedback to patients could include the dissemination for example of information on standards of care or the opportunity to take part in clinical trials. The EuroBioBank informed consent may serve as a template.

The following steps and timelines for integrating existing and building up new national registries were set out: before the end of July, each of the new national registries will decide on the most appropriate "mode of operation". Existing registries will develop a plan for implementing necessary modifications. A plan for technical implementation on the national level will be developed by national registries and supported by the work package leader in Montpellier. Further actions include information and involvement of national patient organizations and clinicians, seek IRB (ethics board) approval for new registries or amending IRB approval for existing registries, translation and adaptation of informed consent, patient information, questionnaire and other documents, hiring of curator personnel, and curator training (November 2007). Furthermore, the group suggested developing a charter for the TREAT-NMD databases that will be presented to the Governing Board. The charter shall set out guidelines and principles including access rights and intellectual property rights and act as a "best practice" model for the future.

Active discussion lists

- partners discussion list
- registries and biobanks
- standardised assessment of animal models
- outcome measures for clinical trials (especially patient's perspective)
- standards of diagnosis and care in DMD and SMA.

If you would like to be involved in any of these discussions or if you know someone who would like to contribute, please let the TREAT-NMD office know (by writing to rachel.thompson@treat-nmd.eu).

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4. Calls for proposals

UPDATE on FP7 HEALTH Work Programme (Call FP7-HEALTH-2007-B)

DEADLINE: 18 September 2007 at 17.00 Brussels local time

Indicative budget: 549 million Euro from 2008 budget

Full details of the 2007 Health call are available at
http://cordis.europa.eu/fp7/dc/index.cfm?fuseaction=UserSite.CooperationDetailsCallPage&call_id=63
If you are interested in applying for any of these calls, please notify Stephen Lynn at stephen.lynn@treat-nmd.eu so we can put you in touch with other partners interested in the same call.

A number of partners are interested in putting together an application for the call below, for the same disorders as those covered in TREAT-NMD, i.e. DMD, SMA, and LGMD/CMD, and an email discussion on this topic has been taking place on the partners mailing list. We would be very interested in hearing from anyone outside the network (from both academic institutions and SMEs) who would be interested in working with us in this area. Interested parties should contact Thomas Sejersen at thomas.sejersen@ki.se.

HEALTH-2007-1.2-6: High throughput molecular diagnostics in individual patients for genetic diseases with heterogeneous clinical presentation. The project should lead to the development of new diagnostic tools exploiting the knowledge of the human genome in combination with advanced read-out technology. Deliverables must be the development of a high throughput, sensitive, reliable and especially cost effective diagnostic test per disease category, which displays clear advantages over currently available diagnostic strategies. Special attention should be given to disease categories with heterogeneous clinical presentation, and/or locus heterogeneity, such as primary immunodeficiencies, muscle disorders, growth deficiencies, hearing or vision impairments and hemoglobinopathies. The project must address quality assurance issues and validation aspects, and should offer opportunities for industrial exploitation, preferably through SMEs.
Funding scheme: Collaborative projects (Small or medium-scale focused research projects).

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5. Upcoming conferences, meetings and workshops

TREAT-NMD Governing Board meeting
Naarden, The Netherlands
1–3 July 2007

MOLEDA SUMMER SCHOOL: "Non-viral gene transfer into muscle and skin"
GENOCENTRE, Evry, France
16–19 September 2007
Number of participants: 150 max
Further info: www.moleda.org

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6. Pick of the articles

The TREAT-NMD newsletter occasionally highlights research and plans for clinical trials that may have implications for patients with neuromuscular diseases. Please note that Phase I/II studies do not prove clinical efficacy – this will require a successful Phase III clinical trial in patients, which this data supports. We also recognise that the data published in the following article support the use of TRO19622 to treat ALS in a rodent model of motor neuron disease.

Trophos Publishes ALS Article in Journal of Pharmacology and Experimental Therapeutics

Trophos Describes Identification, Characterization and Broad Neuroprotective Properties of TRO19622 in Journal of Pharmacology and Experimental Therapeutics

Neurodegenerative Disease Specialists Publish Details of a Novel Drug Candidate for ALS That Targets Mitochondrial Proteins

MARSEILLE, June 19th, 2007 - Trophos SA, a biopharmaceutical company specializing in the discovery and development of drugs for neurological disorders, announced that a publication entitled "Identification and characterization of TRO19622 (cholest-4-en-3-one, oxime), a novel drug candidate for amyotrophic lateral sclerosis" has been accepted and published online in the Journal of Pharmacology And Experimental Therapeutics (J Pharmacol. Exp. Ther. 2007 May 11; [Epub ahead of print]).

Amylotrophic lateral sclerosis (ALS), more commonly known as Lou Gehrig's disease in the USA, is a progressive and fatal neurological disease that is estimated to affect about 100,000 people worldwide. There is no cure for ALS. The only drug approved for ALS is riluzole (Rilutek(R), Sanofi-Aventis), which has been demonstrated to confer some survival benefit to ALS patients.

The studies reported in the paper by Bordet et al., (see below) identify two protein targets of TRO19622 present in the outer mitochondrial membrane suggesting that the compound has potential in a range of additional commercially attractive therapeutic indications involving mitochondrial dysfunction, including painful neuropathies. The publication describes the models of motor neuron disease employed to support the use of this compound to treat ALS, as well as spinal muscular atrophy. TRO19622 is currently in a Phase IIa clinical trial to establish its efficacy as a treatment for painful diabetic neuropathy.

TRO19622 is representative of novel compounds identified using the proprietary neuronal cell screening platform developed at Trophos. In vitro, TRO19622 promotes motor neuron survival in the absence of trophic support in a dose-dependent manner. In preclinical models in vivo, TRO19622 rescues motor neurons from axotomy-induced cell death in neonates and promotes nerve regeneration following sciatic nerve crush. Furthermore, in the SOD1G93A model of familial ALS, TRO19622 treatment improves motor performance, delays the onset of the clinical disease, and extends survival.

TRO19622 binds directly to two components of the mitochondrial permeability transition pore: the voltage-dependent anion channel (VDAC) and the translocator protein (or peripheral benzodiazepine receptor), suggesting a potential mechanism for its neuroprotective activity.

TRO19622 has successfully completed Phase I/Ib studies in both healthy volunteers and ALS patients demonstrating the product is well tolerated, has an excellent safety profile and that once-a-day dosing achieves the predicted exposure level required for efficacy, based on preclinical models. These data support the further clinical evaluation of TRO19622 as a potential treatment for ALS.

"Trophos is proud to have this body of work accepted for publication in a well recognized journal such as JPET," said Rebecca Pruss, CSO at Trophos. "Given the significant unmet medical need in ALS, it is tremendously encouraging that TRO19622 promotes the survival of motor neurons in this extensive battery of preclinical models. These studies, along with the excellent clinical safety profile of TRO19622, provide the basis upon which Trophos plans to initiate a pivotal Phase II/III trial to establish the clinical efficacy of TRO19622 in ALS patients."

Pruss added: "Moreover, we are particularly excited that there is increasing preclinical evidence that the mitochondria-mediated mechanism of action of TRO19622, and other compounds in this class, will have huge commercial potential in other chronic neurological disorders, such as neuropathic pain, and non-neurological conditions, such as ischemia-reperfusion injury and hepatitis."

Author List: Thierry Bordet, Bruno Buisson, Magali Michaud, Cyrille Drouot, Pascale Galea, Pierre Delaage, Esther-Marie Steidl, Delphine Maux, Michel Delaage, Rebecca M. Pruss (Trophos), Natalia P. Akentieva, Alex S. Evers, Douglas F. Covey (Washington University School of Medicine), Mariano A. Ostuni, Jean-Jacques Lacapere (U773 Inserm), Charbel Massaad, Michael Schumacher (UMR788 Inserm), Christopher E. Henderson (Center for Motor Neuron Biology, Columbia University)

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7. Partner-specific items

Governing Board meeting

All Governing Board members should have received the agenda for the upcoming Governing Board meeting in Naarden. If you require a copy, please write to Stephen Lynn at stephen.lynn@treat-nmd.eu. This will be a very busy and productive meeting and many partners have been asked to prepare items in advance. If you would like clarification on any issue, please do not hesitate to contact Stephen at the address above. Various discussion documents and other papers have also been distributed in advance of the meeting.

Posters and presentations for Governing Board meeting

Partners have been asked by Stephen Lynn to prepare and present posters and/or presentations for the Governing Board meeting. Templates are available to download from the private section of the website http://www.treat-nmd.eu/private/.

As a general guide, can we please request that all posters should be printed A1 size (594x841 mm or 23.4x33.1 inches). The poster template page setup is set at A1 size. The posters will be on display from the evening of Sunday 1st July until the close of the meeting on Tuesday 3rd July. The UNEW team are very happy to help you in preparing the content for these posters, so please feel free to contact us.

You will also find on this web page a template for producing PowerPoint presentations related to the network. Please use this template when designing presentations that you intend to give on your activities within the network. We hope you find these templates useful.

Reimbursement guidelines

As the number of TREAT-NMD activities are increasing across the network reimbursement guidelines have been drawn up to help simplify your planning and implementation of TREAT-NMD related meetings and workshops. These guidelines have been posted on the private section of the web site and will be incorporated into the next version of the TREAT-NMD Project Management Manual. Please print-out and read these guidelines – they will help you to correctly identify the source for reimbursement when attending workshops and meetings.

Discussion forums / lists

Would you like us to set up a discussion forum for you on the TREAT-NMD website?
If so, please e-mail rachel.thompson@treat-nmd.eu.

Calls for proposals / funding opportunities

Please forward to us at the Coordination Office any calls for proposals and funding opportunities you receive within your institution. We will then advertise these in the newsletter and on the website.

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8. Send us your news and views!

We strongly encourage all partners and supporters to send their own news and updates and we will be happy to include them in future editions of the newsletter. Please send your contributions to emma.heslop@treat-nmd.eu

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