Care and Trial Site Registry – CTSR
A Powerful Tool for Clinical Research in Rare Diseases

Kirsten König and Jan Kirschner
Dept. of Neuropaediatrics and Muscle Disorders
Universitätsklinikum Freiburg, Germany

TREAT-NMD TGDOC meeting
Leuven, September 2016
CTSR and patient registries

Complementary information

Patient registries:
- exact information on an individual patient
- allows direct contact with individual patients

Care and Trial Site Registry:
- database of neuromuscular centres
- contains only the number of patients in an age group

No linkage between CTSR and patient registry
Number of sites since 2008

- 2008: NMD
- 2009: NMD
- 2010: NMD
- 2011: NMD
- 2012: NMD
- 2013: NMD
- 2014: NMD, both
- 2015: NMD, both
- 2016: NMD, both

NMD: Neuromuscular Disease
both: Both NMD and NDD
NDD: Nonspecific Nervous Disease
340 registered sites worldwide
Patient numbers since 2008
68,000 patients in 51 countries

December 2015

- Duchenne: 15,190
- Becker: 4,260
- SMA I: 1,028
- SMA II: 3,119
- SMA III: 2,392
- LGMD: 8,217
- CMD: 1,870
- CM: 2,580
- FSHD: 5,141
- DM1: 10,128
I. CTSR Usage

Feasibility reports

In 2016:

Two feasibility reports for major pharmaceutical companies

Since establishment in 2007 20 feasibility reports for pharma
II. CTSR Usage

- Surveys/audits to assess care standards
  - Muscular Dystrophy UK
  - Action Duchenne

- Find partners for projects
  - MYO-SEQ
  - Vision DMD
  - ERN

Questionnaires with restricted visibility
Vision DMD

- EU project financed by Horizon 2020
- Drug development of vamolorone (VBP15), an experimental steroid-like drug for DMD
- Feasibility query through temporary questionnaire with restricted visibility to pre-selected sites
Vision DMD questions

Please enter the following contact details:

<table>
<thead>
<tr>
<th>Trial coordinator name:</th>
<th>Jan Kirschner</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial coordinator email:</td>
<td><a href="mailto:jan.kirschner@uniklinik-freiburg.de">jan.kirschner@uniklinik-freiburg.de</a></td>
</tr>
<tr>
<td>Physiotherapist name:</td>
<td>Kirsten König</td>
</tr>
<tr>
<td>Physiotherapist email:</td>
<td><a href="mailto:kirsten.koenig@uniklinik-freiburg.de">kirsten.koenig@uniklinik-freiburg.de</a></td>
</tr>
</tbody>
</table>

What kind of clinical assessments are performed in ambulatory DMD children in clinic and which one in a clinical trial set up only?

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Clinic routine</th>
<th>Only in clinical trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>North Star Ambulatory Assessment</td>
<td>✔️</td>
<td></td>
</tr>
<tr>
<td>Time to run/walk 10m</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Time to rise from the floor</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Does your site have the facility to perform an eye assessment for cataracts and glaucoma by an ophthalmologist/optician or would this be provided by local clinicians, external to your site?

☐ Site has facility  ☐ External ophthalmologist/optician

VISION DMD - Initial Site Questionnaire for MRI

The VISION-DMD project uses MRI end-points to assess the effect of the therapeutic agent VBP-15.

In order to determine whether your site will be able to perform the MRI for the study, we need to collect certain information about your MRI scanner and its software, your scanner operators and physicists. Please ask your MRI specialist to fill out the MRI questionnaire.

Download the questionnaire for MRI here.

Please send the completed questionnaire to jan-dmd-mri@ncl.ac.uk.
EURO-NMD
European network of reference centers for rare neuromuscular diseases

Proposal submitted to the European Commission for Public Health as response to the call for European networks of reference for rare diseases

EURO-NMD will unite 61 of Europe’s leading NMD clinical and research centres in 14 Member States and includes highly active patient organizations.
Potential Networks proposals (06.04.16)

Broad thematic proposals (13)
- Rare auto-immune and auto inflammatory diseases
- Rare Bone Diseases
- Rare Cancers and Tumours Paedriatic
- Rare Eye Diseases
- Rare hepatic diseases
- Rare hereditary metabolic disorders
- Rare malformations and developmental anomalies and rare intellectual disabilities
- Rare neuromuscular diseases
- Rare pulmonary diseases
- Rare renal diseases
- Rare skin disorders
- Rare urogenital diseases
- Transplantation in children

Still initial or unclear proposals (3)
- Rare gynaecological and obstetric diseases
- Rare connective tissue and musculoskeletal diseases
- Rare Cancers and Tumours Adults

Two or more tentative proposals (5)
- Rare endocrine diseases
- Rare Vascular diseases
- Rare Cardiac Diseases
- Rare haematological diseases
- Rare neurological diseases

No known proposals
- Rare craniofacial anomalies and ENT (ear, nose and throat) disorders
- Rare gastronintestinal diseases
EURO-NMD Goals

• Harmonise and implement standards for clinical and diagnostic best practice

• Improve equity of care provision across member states

• Facilitate translational and clinical research

• Harmonise data and samples for research reuse
http://euro-nmd.info/
CTSR and the ERN

• Gather information

Patient population

<table>
<thead>
<tr>
<th>Neuromuscular diseases</th>
<th>Under 18 yrs</th>
<th>18 yrs and older</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>calculated from below</td>
<td>185</td>
<td>101</td>
</tr>
</tbody>
</table>

+ Skeletal muscle disease ORPHA98472
+ Motor neuron disease ORPHA98503
+ Muscular channelopathy ORPHA71864
+ Neuromuscular junction disease ORPHA98491
+ Rare peripheral neuropathy ORPHA98496
+ Mitochondrial disorders Definition ORPHA68380 ORPHA206966

• Disseminate information through special page with restricted visibility in the CTSR or via mail
CTSR Outlook I

• Improve **geographic coverage** of CTSR:
  – Most but not all important neuromuscular centers are registered
  – Some countries are underrepresented

• Closer collaboration with patient registry curators
  – To find neuromuscular centres not represented in the CTSR
CTSR
Care and Trial Site Registry

Welcome to the Care and Trial Site Registry
for neuromuscular and neurodegenerative diseases

To see a complete list of the sites in the CTSR click here.
CTSR Outlook II

- Improve **linkage** between CTSR and patient registries:
  - Currently two separate data sets
  - It is not known at which center an individual patient is seen

- Integrate information about care centre in patient registries
  - CTSR could provide a data file that patient registries could integrate as a dropdown menu
CTSR conclusions

- The CTSR is complementary to TREAT-NMD patient registries and is increasingly used by industry and academia.

- Flexible application, which can be used for country specific monitoring of care sites or finding project partners.

- Improving geographical coverage and linkage between patient registries and the CTSR would further improve the utility of the CTSR.
Thank you

Jan Kirschner

Kirsten König

Contact us: ctsr@uniklinik-freiburg.de