UK SMA PATIENT REGISTRY NEWSLETTER

www.treat-nmd.org.uk/registry

Issue 1 • July 2014•

Welcome to the newsletter for the UK SMA Registry!

Welcome to the first edition of the UK SMA Patient Registry newsletter.

Promising new treatments for SMA are being developed and they need to be tested in clinical trials. When planning a clinical trial, it is very important that suitable participants can be identified and contacted quickly. The registry is becoming increasingly important as it makes it easier and faster to find patients who are potentially eligible for clinical research and trials and it provides the information that researchers will need.

Inside this issue:

Useful Contacts

The UK SMA Patient Registry:
Website: www.treat-nmd.org.uk/registry
E-mail: registry@treat-nmd.org.uk
Telephone: 0191 241 8617

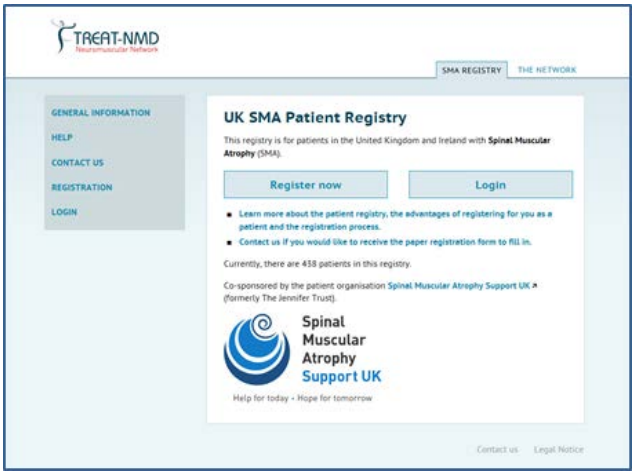
Post: UK SMA Patient Registry
TREAT-NMD Office
Biomedicine West Wing
International Centre for Life
Newcastle upon Tyne
NE1 3BZ

Spinal Muscular Atrophy Support UK
(previously Jennifer Trust):
Website: www.smasupportuk.org.uk
E: supportservices@smasupportuk.org.uk
Telephone: 01789 267520

Agata Robertson is the new curator for the UK SMA Patient Registry. She works in Newcastle with the TREAT-NMD team. Agata is responsible for making sure all of the data in the registry is accurate and up to date. She is your point of contact for everything to do with the registry so please don't hesitate to get in touch her if you have any questions about the registry (contact details above).

1. Registry upgrade

The UK SMA Patient Registry website has undergone some changes which you may have already noticed if you have recently logged in or just looked at the website. This is because the registry has recently been upgraded to make registering and updating details easier. We have also tried to make it easier for people to register and log in by adding these functions to the homepage of the registry website.



What does the upgrade mean to you?

Log in

To log into the registry you now need to enter your e-mail and the password that you chose when you registered.
Login function can be found on the homepage of the registry website.

Informed consent

If you registered before June 2014, you would have sent a signed paper copy of the consent form to the registry curator. As a result of the upgrade, people who sign up to the registry can now consent on-line. This means that when a new patient registers an informed consent form is automatically created for them.
The consent form is personalised, containing the name of the respective patient as well as of the user account owner (if different from the patient). The informed consent is a PDF document, which you can download and print for your own documentation.
Because of the registry upgrade, next time when you log in to update your details on the registry you will be asked to consent online. What you agree to is the same as previously but please do read the information provided before you tick 'I agree' box to make sure that you are still happy to be on the registry. If you have any questions about online consent please get in touch with the registry curator.

What happens if you forget the password?

In the past you had to get in touch with the registry curator if you forgot your password. Now, if you forget your password, you can visit Forgot password web page. There you will be asked to enter the e-mail address with which you registered. You will then receive an e-mail containing a link with which you can reset your password.
If you have any problems with logging in, e.g., if you don't remember which email you used when you registered, please get in touch with the registry curator.

Reminder emails – update your records

It is important you keep your details up to date so now you will receive an email to remind you to update your record once a year.
If anything does change before then, e.g. your contact details or there has been a major change in your circumstances, then please remember to update them in the registry, too.

More information on the website

We will continue to work on the website and improve it. We hope to add more information such as: FAQ, glossary, newsletters and registry leaflet.
If you have any feedback on the registry website then we would love to hear it – please contact the registry curator.

2. Quick registry facts

What is the SMA Registry?
It is a database of genetic and clinical information about people affected by SMA

How is the information used?
To speed up finding patients for clinical trials
To help researchers and doctors learn more about SMA and how many people are affected
To help improve standards of care for people with SMA

Who should register?
Adults and children with SMA and a confirmed mutation in the SMN1 gene who live in the UK or Ireland

How to register?
Create an account so that you can view and update your information at any time
www.treat-nmd.org.uk/registry
If a person with SMA is under 16, a parent or guardian must create an account on their behalf.

3. Is your record complete and up-to-date?

The registry is only as useful as the information it contains so it is important you keep your details up to date. You will be reminded to update your record once a year. If anything does change before then, e.g. your contact details, then remember to update them in the registry as well.

While updating your details remember to check if you have:

Provided us with the genetic report;
One of the most important pieces of information that we ask for in this registry is the patient's genetic report, which we need a copy of. If you as a patient have already got your genetic report, or if you can get it quickly and easily from your doctor or geneticist, then please send a copy to the registry curator when you have got it. If it is difficult for you to obtain it yourself, we will ask your doctor or geneticist for it on your behalf, and in this case you need to let us know contact details of the doctor/hospital where the genetic test was carried out. However, it is useful for us to have these contact details even if you intend to send us a copy yourself.

Completed all the questionnaires;
The self-report online registration also includes a questionnaire; the questions address your genetic mutation and your diagnosis, as well as your physical condition/symptoms including your motor function (ability to sit/walk), how you eat and your respiratory function (breathing ability). The more information we have the more useful the registry can be. The details you provide may help to inform future research and improve standards of care.

4. Registry workshop at the 'Day to Day with SMA' conference

Agata, the registry curator attended the SMA Support UK (previously Jennifer Trust) 'Day to Day with SMA' conference in June this year. At the workshop: 'SMA Reach UK and SMA Patient Registry: what they do and how to get involved' she gave a brief presentation about the registry, a live demonstration of the upgraded registry and explained how the registry links with the SMA REACH project. Some of the questions raised during the session can be found in the FAQ section of this newsletter.
The presentation from the workshop is available on the SMA Support UK website.

5. How has the registry been used?

The UK SMA Patient Registry has already been very valuable for SMA research. It was used for the planning and recruitment of a clinical trial as well as for the academic study that looked at the SMA care standards in different countries. It was also used to provide information to the Medicines and Healthcare products Regulatory Agency (MHRA).

Medicines and Healthcare products Regulatory Agency (MHRA) query

Medicines and Healthcare products Regulatory Agency (MHRA) is the UK authority responsible for licensing medicines for use and for deciding whether a trial can go ahead in the UK.

In 2013 the MHRA was reviewing a clinical trial for SMA in the UK that a pharmaceutical company was considering running. As part of its review process, the MHRA wanted to hear from people with a connection to SMA (doctors, researchers and people with SMA) about their opinions on some aspects of the trial design. The SMA Support UK (at the time called Jennifer Trust for SMA) and the registry were asked to help to send out the MHRA's questions to people with SMA and their families

In July 2013, a webpage was created on the TREAT-NMD website that described the background and the questions being asked in more detail. The link to the questionnaire was sent out to people on the registry. The responses received were then collated into a report by the Jennifer Trust and passed back to the MHRA. We would like to thank everyone who responded to the query.

Further information about the MHRA query can be found on the TREAT-NMD website: http://www.treat-nmd.eu/sma/mhra-queries/

Trophos Clinical Trial

The French pharmaceutical company Trophos carried out a two year-long Phase II clinical trial of the drug Olesoxime in SMA patients. Trophos has recently announced positive results from this trial.

It was an international SMA clinical trial to which UK SMA Patient Registry, alongside other TREAT-NMD SMA patient registries across Europe, has greatly contributed to both planning and the recruitment stages. The trial included 165 Type II and non-ambulatory Type III SMA patients aged 3-25 and it was performed across 22 centres in seven different European countries. Eighteen patients from the UK took part in the trial. Trophos acknowledged a great contribution of the registries to recruiting the number of patients that the company planned to enrol in the trial within less than 9 months.

The trial was testing the effectiveness of Olesoxime - specifically developed as a potential treatment for SMA. Olesoxime was given daily in liquid form, helping oral delivery to young children, and patients were assessed every three months during the study. Olesoxime has shown to protect nerve cells from damage in cell culture, while improving neuronal growth and function, indicating that it may be beneficial to patients with SMA. The promising results of the trial are expected to lead to further testing of Olesoxime as a potential treatment for SMA. Trophos has reported that they now focused on the regulatory steps needed to bring Olesoxime to market.

For further details about the results visit:
http://www.treat-nmd.eu/sma/clinical-research/olesoxime-top-line-results/
http://www.trophos.com/news/FAQ_en.htm

Study looking at the SMA care standards in different countries across the world

The UK SMA Patient Registry has also contributed to the study looking at national SMA registries worldwide. This international scientific study: 'Mapping the differences in care for 5000 Spinal Muscular Atrophy patients, a survey of 24 national registries in North America, Australasia and Europe' was published in the Journal of Neurology earlier this year. The study combined data from the UK registry with data from other registries across the world. It provided some useful comparisons between countries regarding patient numbers and variations in care practices on ventilation, gastric feeding, scoliosis surgery and loss of ambulation (walking) in type III SMA. It also compared the results with the published recommendations on standards on care. This study is of interest not only to people with SMA and their families but also to researchers, clinicians and pharmaceutical companies planning trials.

The study included 5,098 SMA patients in 25 countries. The study showed that there are a number of variations from the standards of care guidelines occurring due to various reasons such as: differences in healthcare systems, financial constraints, availability of specialist care and social or cultural attitudes towards life-limiting diseased.

The study underlined how important the registries are. It showed that the information gathered through the registries is useful for planning and recruitment for clinical trials and also for care and social planning and the development of national plans for rare diseases such as SMA. This study provides the basis for further research in, for example, the quality of life in ventilated SMA patients.

Box 1.

Snapshot of some findings from the international study:

Number of SMA patients included in the study:
- **5,098** SMA patients

Number of registries that contributed to the study:
- **24** registries

Size of the SMA registries analysed:
- the smallest had **3** patients (Macedonia)
- the largest one had **2834** patients (USA)
- UK registry had **368** patients at the time

Number of studies using SMA registries
SMA registries used for **15** studies worldwide

Types of studies that registries were used for:
- clinical research (including recruitment)
- natural history surveys
- epidemiological research
- genotype/phenotype analysis
- mutation data collection
- social and healthcare services planning

Clinical trials
40% of registries used for identifying patients who fulfil the inclusion criteria (feasibility)
60% of registries were used for recruitment
The UK SMA registry was used for both.

A snapshot of some findings from this international study is presented in Box 1.
If you would like to find out more about the study you can go to the TREAT-NMD website:
http://www.treat-nmd.eu/resources/patient-registries/publications/sma/
or contact the registry curator for more information.

6. Research update

Isis Pharmaceuticals

Earlier this year, ISIS Pharmaceuticals has provided an update on interim results from Phase II trials of their gene therapy drug ISIS-SMNRx. The two trials, one in infants with SMA type I and the other in children with SMA types II and III, are both open-label studies designed to test multiple different doses of the treatment.

ISIS-SMNRx is an antisense oligonucleotide that targets the SMN2 "backup" gene, encouraging it to produce more survival motor neuron (SMN) protein in order to replace at least some of that which is missing in SMA.

The data collected from these trials so far indicate that ISIS-SMNRx is safe and well tolerated at all tested doses, and that the drug may positively affect the course of the disease. Dependent on the final outcome of these Phase II studies, Phase III clinical trials are planned for later this year.
Source:
http://www.smasupportuk.org.uk/blog/research/isis-pharmaceuticals-announces-interim-results-of-isis-smnrx-phase-ii-trials

What is gene therapy?
It is a treatment of a genetic disease by repairing or replacing a faulty gene.

Currently three approaches are being investigated as potential gene therapy treatments for SMA:
- replacement of the lost SMN 1 gene in cells
- using small pieces of genetic material, called oligonucleotides , to improve the functioning of the 'back up' SMN2 gene
- delivering neuroprotective proteins to motor neurons to help keep them alive and well functioning

SMA Screening Survey (UK)

Imagining Futures Project called 'The social and ethical implications of genetic screening for SMA' is a 3 year research project led by a researcher at Warwick Medical School, Dr. Felicity Boardman. The project aims to explore the way in which people living with SMA in their family perceive the social and ethical issues that surround population screening for SMA.

At present, in the UK, only families who have a confirmed case of SMA are offered carrier testing and prenatal diagnosis for subsequent pregnancies on the NHS. However, in some countries such as the United States there are discussions about the possibility of introducing screening for SMA to the whole population. Screening for SMA would involve the identification of SMA in the general population, not just within families already affected by the condition.
The Imagining Futures project is designed to explore the way in which families living with SMA feel about the possibility of screening. The study builds on an earlier interview study, conducted in 2006-2010, with 54 people living with SMA in their family which explored their attitudes about the use of prenatal testing and selective termination for SMA. The participants in this study have been invited to be re-interviewed about their experiences since their first interview, and also to describe their views about SMA screening.

Once these follow-on interviews are completed, an online and postal nation-wide survey of families living with SMA will be sent out in September 2014, through both SMA Support UK, and though the SMA Patient Registry. The survey will give everyone who has SMA in their family the chance to participate in the research and have their views on screening for SMA heard. The results of this research will be submitted as research evidence to the UK National Screening Committee in their next review of the policy on screening for SMA in the UK.

For further information about the Imagining Futures Project please visit:
www.warwick.ac.uk/imagining_futures or follow on Twitter at www.twitter.com/imaginingfuture

PTC, Roche and SMA Foundation collaboration

PTC Therapeutics has announced earlier this year that its selected lead compound with potential to treat SMA has entered early stage clinical trials. This is the first drug to reach clinical development coming from the three-way collaboration between PTC, Roche, and the SMA Foundation, started at the end of 2011.

This small molecule drug is able to increase the levels of survival motor neuron (SMN) protein and therefore has potential to at least partially improve the symptoms observed in SMA. The drug will be tested in a Phase I clinical trial in healthy adult volunteers, in order to increase understanding of its safety and tolerability in humans. This potential treatment is to be taken orally (by mouth), meaning that it can be easily administered without specialist equipment or expertise.

Gene therapy research in Sheffield

The research group led by Professor Azzouz (Sheffield University) have developed a new SMA gene therapy in mice that makes use of viruses to replace the SMN protein lost by SMN1 gene mutations. The principle is that SMN1 is packaged into harmless viruses, which can then be injected into SMA patients. These viruses are then able to travel around the body, targeting various cells including the motor neurons, where they produce SMN protein for long periods of time. Using viruses to replace SMN protein in SMA patients is considered to be one of the most promising potential treatments for the disease.

A similar research is also being carried out in the USA where a gene therapy clinical trial has recently started.

SMA REACH UK and UK SMA Patient Registry – update on collaboration

At present much of the data that is collected on people affected by SMA in the UK is held within two national databases: the UK SMA Patient Registry and the Smartnet database. SMA REACH UK is further development of the Smartnet database which holds longitudinal data (involving repeat observations over a long period of time) collected by clinicians at routine clinic appointments.

The key people involved in these databases have explored an opportunity to collaborate. As a result they are now trying to establish a unique access point (portal) which will allow the data from SMA REACH UK and the UK SMA Patient Registry to be exchanged. Data will continue to remain separate in each database but the portal will allow the exchange of anonymised information about patients including diagnosis, medical assessment and management of SMA. The aim is to enable better preparation for clinical trials and to bring together in one place accurate details about SMA and how the condition changes over time. The exchange of this data will allow doctors and researchers to make the very best use of the information available to them to inform decision making and to prepare for clinical trials in the UK.

Natural history data from the SMA REACH UK database would be useful to have alongside the UK SMA Patient Registry data as it would give a clearer idea of the functional abilities and failing clinical trial screening. Only those patients who have agreed by giving their informed consent will have their data exchanged via the portal.

If you have any question about this collaboration please get in touch with the registry curator or visit the SMA REACH website: http://www.smareachuk.com/

7. Frequently asked questions

How often should my data be updated?

You should update your data at least once a year and an automated email will be sent to you to remind you to do this. You will have access to your account and so you can in fact log in and review the data stored on you at any time and also make any updates as and when it is necessary.

If you move house, change your email address, or get a new phone number we would ask that you make sure you update this information in the registry so that we are always able to contact you.

Is my data safe?

All the information is stored in a secure server which is protected in a similar way to online bank accounts. Only specially appointed registry staff can look at your information.

The UK SMA Patient Registry is part of the TREAT-NMD Global SMA Registry, which collects medical information from national SMA registries worldwide. When your data is transferred from the UK SMA Patient Registry to the TREAT-NMD Global SMA Registry, your personal details do not go with it. Your information in the global registry is identified only by a code. You can be sure that your contact details are safe.

What happens if I am potentially eligible for a clinical trial?

If you meet the criteria for a particular trial based on the data held about you in the registry you will be informed about it and provided with some information. If you are interested in the information that you receive about a particular clinical trial, you will be given details to contact the researchers running the trial. If you decide to take part in the trial, you will need to review and sign a separate consent form. You are completely free to make your own decision about any trial we inform you about. If you decide not to take part in a particular trial, your data will still be kept in the registry and we will continue to inform you about other trials unless you tell us not to. Please note that if we tell you about the existence of a trial, this does not imply that we endorse it.

Thank you for reading this newsletter, if you have any feedback or suggestions for the next issue then please contact the registry curator Agata Robertson

E-mail: registry@treat-nmd.org.uk
Telephone: 0191 241 8617
Post: UK SMA Patient Registry
TREAT-NMD Office
Biomedicine West Wing
International Centre for Life
Newcastle upon Tyne
NE1 3BZ

Spinal Muscular Atrophy Support UK
Help for today • Hope for tomorrow
(formerly The Jennifer Trust)

TREAT-NMD Neuromuscular Network

The UK SMA Patient Registry is funded by the Spinal Muscular Atrophy Support UK.

Spinal Muscular Atrophy Support UK is the new name for The Jennifer Trust for Spinal Muscular Atrophy. The decision to change the name has been made after a long period of research and consultation. Spinal Muscular Atrophy Support UK will continue with the same work and services. You can read more about the background to why we have made this change on the website: www.smasupportuk.org.uk/name-change