Genomic Translation for ALS Clinical Care (GTAC) Participant Information Leaflet

Version 1.2
20th December 2016

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

The GTAC Study – an introduction
This study is called "Genomic Translation for ALS Care," or "GTAC" for short. GTAC is an international observational study that will investigate why a person develops Motor Neurone Disease (MND) and why their symptoms present and progress with particular patterns. Motor Neurone Disease is also known as Amyotrophic Lateral Sclerosis (ALS) but in this information leaflet it will be referred to as MND except where it is part of the project title.

Professor Siddharthan Chandran & Dr. Suvankar Pal at the University of Edinburgh are collaborating in an international research consortium (GTAC). The international collaboration is led in the USA by Dr Mathew Harms, Columbia University Medical Centre, New York. The study aims to recruit 1500 participants between centres in the USA and Scotland.

What is the purpose of the study?
We will gather information about your health, environmental exposures over your lifetime, and follow the pattern/progression of your disease over time. This information will be used together with genetic information from your blood to look for factors that determine why motor neurone degeneration begins and how or why it progresses. The study will also store cells from your blood that can be used in future studies.

Can I take part? Yes if you have a diagnosis of motor neurone disease, live in Scotland, are not on invasive respiratory support or non-invasive support for more than 22 hours per day and are not pregnant.

Do I have to take part?
No, and if you do decide to take part you are also free to withdraw at any time and without giving a reason. Deciding not to take part or withdrawing from the study will not affect the healthcare that you receive, or your legal rights.

What does the study involve?
If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You will then be seen by the study team at visits alongside your routine clinical care visits (approximately every three months) for up to three years.

First study visit: We will arrange a separate clinic visit, or see you after a routine clinic visit if this is more convenient for you and clinic space is available. Having given you the information on the study and allowed you enough time to review the information we will discuss the study and answer any questions you have. If you are satisfied and willing to participate, we will ask you to complete the consent form. This is attached as an appendix so that you can read it in advance.

After the consent form is signed, we will take a brief history, recording details about you and your health. This will include a history of the places that you have lived. We will ask you about your general health history, your family history of diseases, medications you have taken or are taking, jobs you have held, places you have lived, hobbies you have participated in, and other lifestyle factors (including tobacco and alcohol use). There will also be questions about your initial MND symptoms, how they have changed over time, and what they are like right now. We will then perform a brief neurological examination similar to that undertaken by your GP or specialist in routine clinical care. We also carry out tests of memory and concentration, along with a few questions about your current emotions.

At the clinic visit we will take a blood sample of approximately 50mls (around 10 teaspoons).

The clinic visit could take up to 4 hours this includes time for refreshments and an opportunity to rest if required.

As part of the study we will also ask your permission to approach your relative, carer or friend (someone who knows you well). With your consent, we will ask your relative, carer friend to complete a short questionnaire (5 minutes) relating to possible changes since onset of MND (You are free to view this before you give consent for us to contact them). This will be completed every 3 months for the duration of your participation in the study. Your participation in the study is not dependent on your relative, carer or friend's participation.

Follow-up study visits: Follow-up visits will give us important information about how your disease is changing over time. The GTAC study will run for three years, so depending on when you are enrolled, you could undergo between 2 and 12 follow-up visits. In most circumstances, these study visits will occur before, alongside, or following your regularly scheduled clinic visits. In rare situations, you may be asked to return at a separate time, but this will be worked out for your convenience. These visits will occur approximately every 3 months but are substantially shorter than the initial visit and every attempt will be made to schedule them around your regular clinic visits. The researchers will ask for updates on your health and other information. Your mobility, strength and breathing will be measured 3 monthly and is often available from routinely collected data which means that you would not be asked to repeat these. Every 6 months, your cognition and emotional functioning will be checked. Follow-up visits should take

less than 20 minutes with the researcher, with any additional questions (by phone or in person) taking up to an additional 40 minutes.

Other possible phone call follow-ups: There may be times when you have to cancel or postpone a regular clinic visit. If your follow up is not in the clinic we may use phone calls to collect the study information about how you are doing.

What will happen to my blood samples and what will they be used for?
The blood samples will be processed, frozen and stored by the Wellcome Trust Clinical Research Facility laboratories in Edinburgh before shipment out to the research centre laboratory in the USA where your blood sample will be analysed to determine the genetic code (whole genome sequencing) and the activity of your genes (RNA sequencing). This will be performed using your de-identified sample.
Any remaining sample will be stored in secure locked freezers for further research studies. Some of the de-identified blood will be used to produce cell lines for use in future research. This means that the laboratory can make more of your DNA for research purposes. The researchers will store your cells indefinitely or as long as they are useful for analysis and research.

Property rights and potential future commercialization: By agreeing to participate in this study, you are giving up any property rights you may have in your samples or other cell lines created from them. It is possible that your samples might be used to develop tests, treatments or cures. There are no plans to provide financial compensation to you should this occur.

Use of samples in future research
We are also seeking your permission to use some of your stored sample in future research projects that could include whole-genome sequencing. This would be on de-identified samples and used only for ethically approved research which may include:-

- Altering some of the DNA within the cells
- Testing in animals to model diseases and treatments
- Developing and testing new drugs and treatments
- Transplanting cells or tissues made from induced pluripotent stem cells (iPSCs) from your blood directly into another patient to treat a disease (known as “regenerative medicine”). At this time, there are no plans to use your iPSCs in this way, but it may be possible to do so in the future.

Such future studies may involve collaboration with other international research centres to share non-identifiable data. Ultimately we hope that the research will lead to the involvement of pharmaceutical companies in the development of new therapies.

Will my taking part in the study be kept confidential?
Yes, all the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard your privacy at every stage. We ask specific permission to let your GP and consultant(s) know that you have agreed to participate. While no individual results will be routinely given out, any clinically relevant incidental findings would be fed back to your GP/treating neurologist.

To ensure that studies are run correctly they are monitored, we will therefore ask your consent for responsible representatives from the Sponsor (University of Edinburgh) and NHS Institution

to access your medical records and data collected during the study, where it is relevant to you taking part in this research.

Who will see my personal data and samples, and how will my privacy be protected?

- **What we collect:** Personal health information recorded will include your date of birth, diagnosis, and details about your disease history & status. Study researchers will need access to your medical records to carry out this research. We also collect samples that allow us to study your genes (DNA) and gene activity (RNA).

- **What we do with your data:** Data from your visit to the Anne Rowling Clinic will be collected on paper and stored securely.

  In order to protect your privacy when your data is transferred onto a computer, a unique study number will be used in place of your name: ***this is called de-identification***. Only key Anne Rowling Clinic researchers will have access to the link between each person's name and code, and this link will be kept in a secure place. The same numeric code used to protect your data will be used to identify all samples.

  Your coded data will be stored on an NHS approved computer system and only anonymised data will be shared with the GTAC researchers outside the local (Edinburgh) research team.

- **Sharing your data and samples:** Your non-identifiable data may be shared with commercial companies in addition to academic researchers. It also means that samples and other cell lines with their accompanying clinical and genetic data may be shared for use in any biomedical research, not just for research about MND.

- **Our privacy standards:** Our management and handling of your data is fully compliant with the Data Protection Act, NHS Lothian, and University of Edinburgh policies.

- No identifiable personally identifiable data will be shared with the USA collaborators.

Are there any risks or disadvantages of taking part?
Giving a blood sample causes momentary discomfort. When taking blood samples there is also a small risk of bruising, and, very rarely, infection.

There are no results returned to you from the sample analysis, however, if the research uncovers any clinically relevant findings this will be fed back to your doctor for action.

What are the benefits of taking part in the study?
There is no direct benefit to you from your participation in this study. However, the knowledge that is gained from the study will help the investigators learn more about MND and the role of genetics and it may also help to develop improved treatments for the disease in the future.

Will I be paid for taking part in the study?
Reasonable travel costs will be reimbursed to a maximum of £10 per subject.

What happens to the results of the study?
The results will be presented to patient groups academic meetings, published in academic/medical journals. Study progress and any interim results will be on the Anne Rowling Clinic website and within the bi annual newsletter. At the end of the study a summary of the results will be made available to all participants who have consented to receive this information. No patient identifiable data will ever be published.

What if I change my mind? You can withdraw from the study at any time without your medical care or legal rights being affected. You may also request at any time that all your biological samples be destroyed. This can be done either by calling the research team at 0131-465-9517 or by writing a letter to Professor Siddharthan Chandran, Anne Rowling Regenerative Neurology Clinic, 49 Little France Crescent, Edinburgh, EH16 4SB. If you chose to do this a sample destruction form will be sent to you to sign, along with a prepaid return envelope so that we have a record of your request. Should you withdraw from the study, any information or research results collected up to that point will be maintained. You should also know that if you change your mind and withdraw from the GTAC study, we would destroy any remaining frozen samples but may be unable to retrieve samples if they have already been shared.

Who is organising the research and why?
This study has been organised by the University of Columbia and sponsored by University of Edinburgh and NHS Lothian. The study is funded by The Amyotrophic Lateral Sclerosis Association (ALSA).

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee. A favourable ethical opinion has been obtained from South East Scotland Research Ethics Committee 2. NHS management approval has also been obtained.

Further questions?
If you have further questions, comments or concerns, you can call the study team on 0131-465-9517 (answerphone available if all staff are busy).

If for some reason you do not wish to speak to the investigating team, you may contact an independent Consultant Neurologist, Dr Peter Connick, Anne Rowling Regenerative Neurology Clinic, Little France Crescent, Edinburgh, EH16 4SB, (0131-465-9500).

If you wish to make a complaint about the study please contact NHS Lothian:
Patient Experience Team, 2nd Floor, Waverley Gate, 2 - 4 Waterloo Place, Edinburgh EH1 3EG, Tel: 0131 536 3370, **feedback@nhslothian.scot.nhs.uk**.

What happens to data and samples for participants recruited in the USA?

As we will not be sending identifiable information (e.g. name, date of birth) from the UK, this does not directly apply to participants recruited in the UK. We therefore provide the information below for completeness only.

"Data from this study will be stored in a data repository at the Massachusetts General Hospital (MGH) Neurological Clinical Research Institute (NCRI). The purpose of this data repository is to capture and store data for neurological clinical research and then combine these data with data from other studies and share the aggregated dataset with researchers who might use it to advance research and understanding of neurological disease.

For this research project, some identifiable information may be collected and stored in the database. This might include information like your date of birth or the date your symptoms began. At the conclusion of this project, the data will be aggregated with data from other studies will then become available for sharing with other researchers.

Global Unique Identifier (GUID):

As part of your participation in the study, a unique subject number, GUID will be assigned to you that will allow researchers to see if you have been involved in more than one research study. If you have participated in more than one study or database, this unique subject number will help connect information across studies. This subject number will also allow your data to be combined with data from other research studies to increase the likelihood of meaningful analysis. This unique subject number can be shared with other investigators when your data is shared and may make it possible for a study doctor who used this unique subject number in another study that you took part in to identify you."

Thank you for taking the time to read this information sheet.