Patient information sheet: Light The Way

Study Title:
Providing access to genetic screening for amyotrophic lateral sclerosis-causing variants and evaluation of perceived benefits arising from an online portal for individuals at risk of genetic ALSand/or frontotemporal dementia (ALS/FTD) in the United States and United Kingdom

Summary of the study:

In this research study we will use information from you and your genetic test result. We will only use information that we need for the research study. We will let very few people know your name or contact details, and only if they really need it for this study.

Everyone involved in this study will keep your data safe and secure. We will also follow all privacy rules.
At the end of the study we will save some of the data in case we need to check it AND/OR for future research.
We will make sure no-one can work out who you are from the reports we write.

The information below tells you more about this.

Description of the study:
This study is intended to identify patients who are genetically at risk of ALS. These people may have a medical diagnosis of ALS/MND, symptoms of ALS/MND or have a family history of ALS/MND. The study involves the collection of saliva and questionnaire responses in order to identify genetic markers that are associated with ALS.

If you choose to take part, you will be asked to complete a baseline survey, attend genetic counselling appointments, and you will be sent an at-home DNA saliva test for the purpose of providing genetic data. If you have already undergone genetic testing for ALS/MND and you would like to upload your test results, you will be offered post-test genetic counselling to address any questions you may have in a safe, supportive space. If you have not previously had genetic testing for ALS/MND, you will be invited to complete a 20-minute educational module that will explain the genetics of ALS, what genetic testing involves and whether it is right for you, and what to expect during the process of undergoing genetic testing.

Additionally, you will receive a pre-test genetic counselling appointment and post-test counselling appointment, where you will receive your genetic test results. Finally, you will have the option of completing research surveys to evaluate your experience of genetic counselling and testing for ALS/MND, and the impact this has had on you.

This study will aim to enrol up to 1,000 individuals into the Light The Way program, and to offer genetic testing for ALS/MND to up to 200 participants with a medical diagnosis of ALS/MND, symptoms of ALS/MND or who have a family history of ALS/MND.

Why is this study being done?
Access to genotyping and genetic counselling for ALS/MND is inconsistent in clinical practice. This study will test for ALS-causing genetic variants in patients with a diagnosis, symptoms or family history of ALS/MND. This will help us understand the prevalence of ALS-causing genetic variants in the USA and UK population, and allow us to explore the psychological impact of receiving education and support for those at risk.

With the support of the scientific community and people at risk of ALS/FTD, we developed an online platform, Light The Way, to offer those on this journey the education, counselling, support, and connection to research that they need. Users who test positive for a known variant, such as SOD1, C9orf72, or FUS, will be updated with additional opportunities to participate in research and clinical trials, education on ALS/MND variants and family planning, and provided with information about treatments as they become available.

When conducting genetic testing for ALS/MND, it can also be useful to test for genes associated with similar, or related conditions which can co-occur in families. One such gene is ATXN2, which is rarely found in families with spinocerebellar ataxia type 2 (SCA2), ALS, or both.

We now know that there is an overlap between ALS/MND, which mostly affects the motor neurons, and frontotemporal dementia (FTD), which mostly affects the brain. Increasingly, the two diseases are considered a spectrum, known as ALS/FTD. When conducting genetic testing for ALS/MND, it can also be useful to test for genes associated with FTD, which can co-occur in families. Examples of such genes are C9orf72, GRN, or MAPT, which represent the three most common causes of genetic FTD.

Who is eligible for this study?
You must meet all of the following criteria to be eligible for this study:

- All participants aged at least 18 years old.
- Willing and able to sign up and provide informed consent online via the Sano Genetics Platform.
- A medical diagnosis of ALS/MND, **OR** symptoms of ALS/MND **OR** a family history of ALS/MND.
- Resides in the United Kingdom or United States of America.
- Fluent in English or Spanish.

What does participation in this study mean?
You will be asked to provide informed consent to participate in the study and to fill out a short pre-screening survey to confirm you are above 18 years old and residing in the United States or United Kingdom.

If you are eligible to take part in the study following the pre-screening survey, you will be asked about your experience with ALS/MND. This will include symptoms, diagnosis and family history. Additionally, you will be asked to complete pre- and post test counselling appointments, and to complete an educational module and order an at-home DNA saliva test. Optionally, you will be asked to complete follow-up surveys to evaluate the experience of undergoing genetic counselling and testing for ALS/MND.

Please note that by joining the study, you are agreeing that your de-identified/pseudoanonymised data may be shared with third parties including academic researchers, non-profit researchers, and for-profit companies we are working with. Access to your identity is restricted solely to authorised personnel at Sano who have received data training, and such access is granted for specific purposes, such as the generation of your individualised report.

This study is exploratory and non-interventional observational patient-finding study, as such there are no therapeutic interventions (medications or treatments) involved.

What should I expect if I decide to take part?
If you decide to take part, you will be asked to complete a pre-screening survey.

If you have previously had genetic testing for ALS/MND, you will be asked to upload a copy of your existing genetic test results. We will then review your genetic test results and, if we are satisfied that these results meet our criteria, you will be offered access to no-cost, online genetic counselling.

However, if we feel that your previous genetic test does not meet our criteria or if you have not previously had a genetic test, you will be asked to complete a short educational module to better understand genetic testing, and it is right for you. If, having understood the risks, you would like to proceed you will be offered an online, no-cost, pre-test genetic counselling appointment.

During this appointment, you will meet with a qualified genetic counsellor to discuss your specific situation, and further explore the risks associated with genetic testing. At the beginning of this appointment, you will need to show a form of photo identification to your genetic counsellor to verify your identity. If after your pre-test genetic counselling appointment you would like to proceed, you will be invited to order a genetic testing kit via our platform. Once you receive your kit, please carefully follow the instructions provided. Using our pre-paid shipping packaging, you will ship your completed test kit directly to the laboratory.

Once the laboratory has received your sample, we will aim to return your results to you within 6-12 weeks. When your results are ready, you will be notified via email. However, before we are able to share your results with you, you will be asked to book an online, post-test genetic counselling appointment. During your appointment, the genetic counsellor will discuss your results with you. After this appointment, your results will be ready to download from our site within 3-5 business days.

Are there costs to participate?
There are no costs to participate in this study. All testing and genetic counselling is completely free of charge, and the sample collection kits will be provided with pre-paid postage so you do not have to pay for returning the sample collection kits in order to take part.

When will I get my genetic test results back?
After providing a saliva sample for genetic analysis, the results are typically available within 6-12 weeks from the time the lab receives your sample. It's important to note that receiving your genetic test result is optional, and you have the choice of whether or not to receive them. If you do choose to receive your genetic test result, a genetic counsellor will disclose the findings to you. Please be aware that the timeframe mentioned is an estimate and may vary depending on various factors, including lab processing times and any unforeseen circumstances.

What are the possible outcomes of my genetic test result?
You will be provided with a report on the test carried out as a part of this study that indicates no significant variant was identified, a significant variant was identified or a variant of unknown significance (VUS) was identified.

If your result indicates no significant variant was identified, this means a genetic cause was not found. This does not mean you do not have or will not continue on to develop ALS/MND. This only means that a genetic cause for ALS/MND was not found.

If your result indicates a significant variant was identified this means that a genetic cause for ALS/MND was found. However, it is critical to note that this result is not a diagnosis of ALS/MND. This result would indicate you are at increased risk for developing ALS/MND. If you receive this result, you should consult with your physician about next steps. Some genetic results may have implications for family members and it is recommended this be discussed with a genetic counsellor.

If your result indicates a variant of unknown significance was identified, this means a genetic variant was found. However, it is critical to note that we are not sure whether it is or will be a cause of ALS/MND. Uncertain results or variants of unknown significance (VUS's) occur when genetic variants are detected in known or suspected ALS/MND causing genes, but there is not enough evidence to confirm if they are connected to an increased risk of developing ALS/MND. We typically keep an eye on these uncertain findings over time, because our interpretation can change.

What are the risks or inconveniences of the study?
The study is observational, so there is minimal risk to you from taking part. Any information that you provide will not be shared, except in an anonymous and aggregated format (no one will know that this information relates to you). Potential risks, disadvantages, or inconveniences are detailed below:

1. While learning about the genetic risks associated with ALS/MND, awaiting test results, or learning about your genetic status, you may experience elevated levels of anxiety, and concerns about the future and the potential implications for family members. You will be supported throughout this process by experienced genetic counsellors who will be able to offer education, support and advice specific to your situation.
2. If you choose to receive your genetic test results you may face issues with health insurance, life insurance, or other forms of insurance. Your pre-test genetic counselling session with a genetic counsellor will advise you on how to mitigate these risks.
3. Although rare, there are cases of employers discriminating against carriers of disease-causing mutations. There are various legal protections in place but these vary depending on where you live and the nature of

your employment. Your pre-test genetic counselling session with a genetic counsellor will advise you how to mitigate these risks.

4. To enrol in this study, you will be asked to complete a pre-screening survey which may be an inconvenience to you due to the time required. However, we expect this process will take no longer than 30 minutes to complete. You may be asked to complete future surveys which may similarly present an inconvenience due to the time required. However, we aim to ensure that all surveys - beyond the pre-screening survey - take less than 15 minutes to complete.
5. You will be asked to complete an at-home saliva DNA test, which may present an inconvenience. We expect this will take you less than 15 minutes, and all return postage is paid for.
6. If you have not yet undergone genetic testing for ALS/MND, you will be asked to complete pre-and post test genetic counselling appointments which may present an inconvenience. We expect this will take you 30 minutes per session.
7. At the beginning of your first pre-test counselling appointment, you will need to show a form of photo identification to your genetic counsellor. Accepted forms of identification include:
    a. A current passport (any nationality)
    b. Biometric Residence Permit (UK)
    c. Current driving licence photocard (full or provisional)

You will be told about any new information that might change your decision to be part of this study.

What are the benefits of the study?
You will receive access to your DNA data, educational modules, genetic counselling sessions, as well as the chance to join further research studies via our platform.

You will be participating in important research into ALS/MND which we hope will allow researchers to gain a better understanding of the genetics of ALS, and contribute to the development of future treatment options.

Where will my samples be stored?
Your biological samples will be transferred to the United States for genetic analysis and storage. The retention periods of biological samples and study data is maximum 5 years and 20 years respectively.

How will we use information about you?
We will need to use information from you and your genetic test results for this research project.

This information will include your:

- Name
- Contact details
- Address
- Date of Birth
- Identifiers held by research and delivery partners, such as laboratories, data processing partners and logistic operators.

People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure.

Some of your information will be sent to the United States, where the rules regarding storage may be less restricted than the UK. However, they must follow our rules about keeping your information safe. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

This study involves research and delivery partners, such as laboratories, data processing partners and logistic operators. To deliver the study we will need to share your Personal Information with some of these partners. We will only share the minimum information with these partners to undertake the task they are performing.

Your Study Data (the answers that you provide in surveys and your genetic test results) will be combined with those of others participating in the program to create a de-identified/pseudo-anonymised data set so that you cannot be re-identified by researchers. This de-identified/pseudo-anonymised data set may be used to support future ALS research by researchers at academic institutions, non-profit organisations, and for-profit companies.

The study staff at Sano may share the records generated from this research with other Sano staff on an as-needed basis. This information is shared so the research can be conducted and properly monitored. The people receiving this information are required to protect it and your information may not be re-disclosed without your permission.

Information you provide in the prescreening questionnaire will be shared with Grey Genetics who are responsible for providing genetic counselling.

Saliva samples you provide will be used to collect DNA for genetic testing. Remaining DNA samples will be stored for up to 20 years, for the scenario where further research is required on the samples.

We take sample security and patients' privacy very seriously. All samples will be kept secure according to international standards, overseen by ethical review. All institutions partnered on this study have adopted these standards and use them routinely, and comply with the Human Tissue Act 2004 and all other relevant regulations and legislation, including the General Data Protection Regulation (GDPR).

Samples stored after this study ends will be stored in line with all relevant legislation, this may be in a secure central repository outside the UK or US. If you wish to find out further information on how we are using samples please speak with a member of the study team.

What are your choices about how your information is used?
You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Who can answer my questions about this research?
Take as much time as you need before you decide to participate in this study. We will be happy to answer any questions whether via email, phone or video call.

If you would like to contact us by phone, you can call us on 020 4525 1999. Our lines are open 10AM-6PM GMT. If you would like to arrange a video call with us, please get in touch with us through our 'live chat' function on your Sano user feed.

If you have any questions, concerns or complaints about the research, or if you think you have been harmed as a result of joining this research, you may contact the researchers who will do their best to help.

Where can you find out more about how your information is used?
You can find out more about how we use your information
at www.hra.nhs.uk/information-about-patients/

- by asking one of the research team through our "live chat" feature
- by sending an email to [contact@sanogenetics.com], or [dataprivacyofficer@sanogenetics.com]
- by ringing us on [020 4525 1999.].

Can I stop participating in the study?

Your decision to take part in this study is voluntary. You will not be penalised or lose any benefits to which you are otherwise entitled if you decide not to participate or if you decide to stop participating at any time. You do not need to provide a reason for withdrawing from the study.

You may withdraw completely from the study at any time, and withdraw the data and samples collected up until the point of withdrawal from use in any future analysis. However, any analysis or interim results that included your information prior to withdrawal cannot be undone.

Can I be removed from this research without my approval?
Your part in this program may be stopped at any time by the researchers without your approval for any reason, including but not limited to:

- If it is in your best interest
- You do not consent to potential changes made in the program plan (if applicable)

Who is organising and funding the study?
The study has been organised and sponsored by Sano Genetics and funded by Sano Genetics and Innovate UK.

Will I be paid for taking part in this research?
You will not be paid for taking part in this research.

This research may support the discovery of future medications that have commercial benefit. Participants will not benefit financially if commercialisation of research findings are successful.

How will the consent process work?
The consent process will be totally electronic via the Sano Platform. Participants must be able to access a computer to complete the consent form and participate in the study. All information relating to the study will be available via the Sano Platform.

Who has reviewed the study?
All research is reviewed and approved by an independent group of people, called a Research Ethics Committee (REC), in order to protect the rights of the people participating in the research. This study has been reviewed by The South West - Frenchay Research Ethics Committee and they have given a favourable opinion of the study. Approval does not guarantee that you will not come to any harm if you take part. However, approval means that the committee is satisfied that your rights will be respected, that any risks have been reduced to a minimum and balanced against possible benefits, and that you have been given sufficient information on which to make an informed decision.