Information Form Parent / Guardian (6-16yrs)
PITMS (PIS02)
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Principle Investigator: **"Insert Site PI"**

Predicting Individual Treatment responses towards personalised medicine in Multiple Sclerosis (PITMS)

Introduction

We are inviting your child to take part in a research study based at the Institute of Neurology in London. Before you decide whether or not they would like to take part, it is important that you understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is unclear or if you would like more information. Please take time to decide whether or not you wish them to be involved. Thank you for reading this.

What is the purpose of this study?

There are many disease modifying treatments which can be started to reduce the risk of relapses. Some people respond well, whilst others do not and continue to develop new symptoms, or develop side effects, and, therefore, need to change medication. Your child's Neurologist cannot predict which drug will work best for them. The decision about which drug to start taking, as you have experienced, is currently very complicated and is based partly on personal preference. For example, a patient may prefer to take a tablet rather than have an injection.

Many elements that may influence treatment response, such as genetic factors, blood biomarkers, MRI markers, etc., are not currently considered when choosing a medication. This is suboptimal, and the decision of which treatment to start should be based on whether it is likely that a person with MS is going to receive benefit from that specific medication. At the moment, the doctors cannot predict what the best treatment is for an individual patient.

The aim of this research is to develop a computer tool that predicts whether an individual patient will respond to a medication by using special mathematical models that learns from the patient's individual MS profile and make predictions about the future. These special mathematical models will consider all the elements that constitute the individual disease profile (demographic and clinical information, life-style, diet, genetic factors, comorbidities, MRI scans).

This study is a crucial step towards “personalised medicine”, which means to be able to prescribe the right medication for the right patient

In order to achieve this aim, we need to collect as much data as possible, and therefore all adults with MS starting a disease modifying drug at UCLH, and all children with MS starting a disease modifying drug at the sites of the UK Paediatric Neuroinflammation Service (which are Great Ormond Street Hospital, Evelina London Children’s Hospital and Birmingham Children’s Hospital) will be invited to take part in this study.

We aim to collect as much data about the manifestations of MS that may influence individual treatment response; these include demographic and life-style factors, blood tests, genetics, clinical examinations, and MRI scans. This will then generate a tool which gives the probability that an individual patient will receive benefit from a particular treatment.

Why have they been chosen? Are there reasons why they cannot take part?

Your child has been chosen because they have been diagnosed with multiple sclerosis (MS) and are going to start taking a disease modifying drug, which aims to reduce the risk of bouts of symptoms (called relapses) and progression of neurological problems. Any disease modifying drug is also expected to reduce the risk of new lesions on MRI scans.

Do they have to take part?

It is up to you to decide whether or not they should take part. Their participation is entirely voluntary. If you agree that they should take part, we will then ask you as their parent or guardian to sign a consent form. If you decide that they should not take part in the study, or to withdraw them once entered, you do not have to give a reason for your choice and this will in no way affect their medical care.

What does the study involve?

Once you have confirmed that you would be happy for them to participate in this study we will discuss the study visits and procedures in more detail. Participation in the study will not change the choice of their medication, and they will start the treatment which has been chosen together with you and their neurologist. They are also able to change medication while on the study if this is deemed appropriate by their clinical care team.

It is important that you understand that most of the time the activities for the study are part of their ongoing clinical care, because they have started on a treatment. As part of their clinical care they will be coming back to the hospital for routine follow-ups with clinical assessments and MRI scans, during which we would include collection of some research data.

If you did withdraw them from the study they would continue with all the elements that are part of their clinical care but would be able to stop the extra research elements, which are: a few questionnaires, and provision of a small amount of extra blood which will be taken with their clinical care safety bloods. In total this is a few teaspoons. The research sample will be used for genetic tests, since we know that genetic and immunological factors may influence their MS and their response to treatment.

Once you have read the information and had a chance to ask the research team questions we will get you to sign a parental / guardian consent form. Once copy will be given to you, along with this information sheet and a copy will be kept for our records.

The visits in clinic will be very similar to that of any patient with MS initiating a treatment, with the addition of some extra examinations, some study questionnaires, a slightly longer MRI scan and a very small extra amount of blood for genetic testing and immunology research.

The MRI scan obtains pictures of their brain and spinal cord using a strong magnetic field and radio waves. The scanner itself looks like a large tube, open at both ends, which they lie in. As the scanner works it makes loud clicking and knocking noises, but with the aid of earplugs (which will be provided) these noises will be reduced. The clinical care component of the MRI requires 10mins of actual scanning, rest breaks are allowed as needed. For the baseline visit only, we acquire an extra 20mins of scanning, a total scanning time of 30mins. Meaning we expect the baseline MRI appointment to take around 45mins to an hour, but for the other visits we expect it to be approximately 30mins with breaks. If they are unable to undergo an MRI scan this will be excluded.

The Clinical Assessment will be very similar to what they would have in a routine neurology clinic appointment. We will ask you as their parent or guardian some questions about their health, which is routine as part of their clinical care. We will then undertake a physical examination, during which we will test their vision, and assess movement and sensation throughout their body. We may also measure their walking speed and assess how nimble their arms are. This assessment usually takes one hour.

The Neuropsychological Assessment will test their memory and thinking, and assess their mood. To do this, we will ask them to have a go at some memory tests, sums, a few puzzles, and ask them a little about their mood. This will take about 30 minutes***,*** with rest breaks as needed.

Bloods Samples *a* sample of their blood (via venepuncture) will be taken for the purpose of the study. They will NOT undergo any additional procedures to obtain these samples, we will only ask for a small amount of extra blood to be taken during

routine hospital venepuncture. The total amount of blood taken is a couple of teaspoons.

It is worth you knowing that

- Blood samples are taken in all cases of MS as part of routine hospital investigations.
- Blood samples are repeated over time once a patient with MS starts a new medication to check whether there are any safety issues.
- A small amount of their study samples will be stored in a registered Human Tissue Act licensed biobank (a secure place for future use) for possible further testing including
    - DNA analysis,
    - immunology testing,
    - neurofilaments levels.

DNA (deoxyribonucleic acid), is found in all cells of the body, and contains the genetic information for the development and working of human beings. Analysing blood samples will allow us to find out the relationship between our environment (exposures) and our personal susceptibility (genes). We may also come up with genetic tests that predict the positive response to a medication. Any results related to genetic testing in patients with MS at this stage are research findings and are not a clinical test. The neurofilaments represent the structure that supports the neurons, so an increased level of neurofilaments in the blood indicates that there has been a large amount of neuronal loss. This may indicate that the drug has not been effective and in future can help patients to avoid taking medications which are not necessary.

It is expected that the total clinic visit, including the MRI scan, will take around 2 ¼ hours. There will be as many breaks as your child would like during the visit and we will try to make your child as comfortable as possible.

Follow up

The design of the study includes a baseline visit, with clinical and MRI assessments, and follow-up visits after 6 months and 18 months. These are routine clinical care follow-ups appointments which will be just slightly longer to allow for the research elements.

At each visit the same clinical assessments, MRI scans and questionnaires will be collected. These assessments will chart their physical condition, but clinical

questionnaires will also give us information on factors such as their progress, quality of life, diet and wellbeing.

The blood tests for genetic testing will only be done at the baseline visit, since the genes do not change over time. The extra blood for neurofilaments and neuroimmunology research, which looks at how the immune system is affected in neurology conditions such as MS, will be collected at each time point at the time of your child's routine blood tests.

Visit Times

	Baseline	6months	18months
Consent	20mins	5mins	5mins
Clinical Care	20mins	20mins	20mins
Research Elements	45mins	45mins	45mins
Brian MRI	20mins	30mins	30mins
Spinal Cord MRI	25mins	0	0
Approx. Visit Time **(with breaks setup etc)**	**2 to 2 ½ hrs**	**1 ½ to 2 hrs**	**1 ½ to 2 hrs**

Travel Expenses

We may also on occasion need to ask your child to attend outside their normal clinic appointment in which case we will be able to pay reasonable travel expenses that you may incur as a result of your child taking part in this study. This includes standard class travel and or 0.40p per mile if you are going to drive.

What will happen to the results of the research study?

We will aim to publish the results of this study in an appropriate medical journal. Your child will not be identified by name in any report or publication. The results of the study will also be presented in National and International meetings. All Participants will be notified about the outcome of the study via the QSMSC newsletter and website.

What are the benefits?

Your child may not directly benefit from this research study, although we hope that they will be getting benefit from the treatment that has been decided as part of their clinical care. It is also likely that you all may experience benefit just by them being involved in this study as you may gain a better understanding of their disease and from the interaction with our research team. We also hope you will all gain satisfaction from knowing that you are helping future patients by helping us take this crucial step towards "personalised medicine", which means to be able to prescribe the right medication for the right patient.

What are the risk?

Some people may feel a little claustrophobic when they are in the scanner, however your child will always be able to speak to the person controlling the scanner via an intercom, and they will stop the scanning session at any time if asked to do so.

Very occasionally during scans people also experience a mild tingling or twitching feeling in their body, arms or legs. This is harmless, but if it happens and causes your child any distress, the scanning session can be stopped.

Will taking part in this study be kept confidential?

If you agree for your child to participate, you will be given this information sheet to keep and you will be asked to sign a parental / guardian consent form. You will be given one copy of the consent form; one copy will be kept by the study team. Your child's hospital may keep an additional copy as part of their clinical notes.

UCL is the sponsor for this study based in the United Kingdom. We will be using information from your child's medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after their information and using it properly. UCL will keep identifiable information about them for 20 years after the study has finished.

During this study, we will access some of their personal details (such as their name and date of birth) from the NHS clinical system. All of this data will be treated as *strictly confidential,* and will only be used for medical research purposes. This data will remain in the NHS clinical system linked by a unique study code. Research data identified only by their unique study code will be held on secure NHS and UCL computer systems. Storage of the data from this study will be the responsibility of the UCL Institute of Neurology, access will be restricted to the researchers involved in the study, as well as the authorities involved in regulating our work. Access to all these computers and workstations requires the use of a personal username and password, as well as being in a secure environment.

Their rights to access, change or move their information are limited, as we need to manage their information in specific ways in order for the research to be reliable and accurate. If you withdraw them from the study, we will keep the information about them that we have already obtained. To safeguard their rights, we will use the minimum personally-identifiable information possible.

All the information about their participation in this study will be kept confidential in accordance with GDPR. Participants can review the UCL Privacy notice at the link below or request a copy from uclh.qsmsc@nhs.net.
https://www.ucl.ac.uk/legal-services/privacy/participants-health-and-care-research-privacy-notice

You can find out more about how we use their information by contacting data-protection@ucl.ac.uk.

What will happen if I don't want them to carry on with the study?

This research is voluntary and you are free to withdraw your child at any time, without giving a reason. Data collected up to this point will be included in the trial analysis.

What if there are any problems?

If you wish to complain, or have any concerns about any aspect of the way you or your child has been approached or treated by members of staff you may have experienced due to their participation in the research, you should ask to speak to the researchers who will do their best to answer their questions. If you are still not happy then please contact: Prof. Olga Ciccarelli, Chief Investigator at olga.ciccarelli@nhs.net or by calling 0203 108 7415.

All professional staff involved in the study hold professional indemnity to work within NHS Trust. In the event that your child is harmed during the research and this is due to negligence then you may have grounds for legal action for compensation against their NHS Trust but you may have to pay their legal costs. National Health Service or UCL complaints mechanisms are available to you.

Please ask their research doctor if you would like more information on this. In the unlikely event that you are harmed by taking part in this study, compensation may be available to you. If you suspect that the harm is the result of the Sponsor's (University College London) or the hospital's negligence then you may be able to claim compensation.

Claims should be made in writing to Professor Ciccarelli who is the Chief Investigator for the research and is based at UCL Queen Square Institute of Neurology. The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this. NHS Indemnity does not offer no-fault compensation i.e. for non-negligent harm, and NHS bodies are unable to agree in advance to pay compensation for non-negligent harm.

Independent Complaints Advocacy Service (POhWER ICAS)

ICAS is an independent organisation that gives help, advice and support to people who have a complaint about the NHS. Contact them on 0845 120 3784 for details of their local office. www.pohwer.net

What information will be held?

If you agree for your child to participate, you will be given this information sheet to keep and you will be asked to sign a parental/guardian consent form. You will be given one copy of the consent form; one copy will be kept by the study team. Your child's hospital may keep an additional copy as part of their clinical notes. As this

document contains your details is considered personal information and is covered under the GDPR.

All data will be treated as *strictly confidential,* and will only be used for medical research purposes. Some or all of this data may be held on NHS and UCL computer systems. Storage of the data from this study will be the responsibility of the UCL Queen Square Institute of Neurology, and access will be restricted to the researchers involved in the study, as well as the authorities involved in regulating our work. To enhance confidentiality, the MRI scans you have will be labelled with a unique identification number rather than their name and only suitably qualified and authorised people will be able to link this code number with their personal details.

On completion of this study, research records will be retained for at least 20 years, and when they are destroyed this will be by confidential procedures. We will keep a permanent record of the fact that you have had an MRI scan, along with the relevant dates and technical details, as these form a part of the MRI scanner's operating and safety record. If you are taking part in any other studies within the NMR Research Unit, we may want to compare the data collected from this study with the data collected from the other studies. If you are not happy for this to happen then you can let us know. Under these circumstances we will keep their research data until all of the studies have been completed. We will keep their contact details to contact you should further studies be planned that we feel you may like to be considered for.

We would also like to include fully anonymised data in open source environments which allows continued development of new models and MRI image analysis methods in MS, which could be applied in future clinical trials of potential new treatments.

Who is organising and funding this study?

UCL is the sponsor for this study.

Funding for the study has been provided by the National Institute for Health Research (NIHR.ac.uk) and the UK MS Society.

Who has reviewed the study?

The study has been approved by the Health Research Agency (HRA) and the Wales 6 Research Ethics Committee. Capacity to conduct the study at this site has been confirmed by the “Insert Local Site Details”. The reference quoted on the first page is issued by the REC that approved this study.

What if I still have questions?

If you have any other questions then please get in touch, by either email or phone with any of the following:

Chief Investigator (based at UCL QS IoN)
Prof. Olga Ciccarelli
o.ciccarelli@ucl.ac.uk
olga.ciccarelli@nhs.net

Research Manager
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Principal Investigator
"Insert Local Site Details".

Research Nurse
"Insert Local Site Details".

Along with this **Parent / Guardian** Information Sheet please use the following

For children **12 to 16**
- Information Sheet **PIS03**
- Consent Form **ICF02**
- Assent Form **ICF03**

For children **6 to 11**
- Information Sheet **PIS04**
- Consent Form **ICF04**
- Assent Form **ICF05**