UNIVERSITY OF LIVERPOOL

Participant Information Leaflet

Study title: Fibromyalgia And Refractory pain in Rheumatic diseases (FARR)

Version2 Date:13/01/2023 IRAS ID: **319560**

We would like to invite you to take part in a research study conducted to better understand Fibromyalgia (FMS) syndrome in patients diagnosed with Rheumatic diseases. Before deciding if you'd like to take part, it is important that you fully understand why this research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others including friends and family if you wish. Please do not hesitate to ask us if there is anything that is unclear or if you would like more information.

Purpose of the study

Fibromyalgia Syndrome (FMS) is a severe chronic pain syndrome diagnosed in 2-5% of the world population. Patients suffering from FMS experience widespread pain associated with different neurological symptoms such as fatigue, anxiety, and depression. People often develop FMS without a clear cause whereas some patients may have experienced a psychological or physical trauma. We do not understand what causes FMS and only few effective treatments exist.

We have recently found in patients with FMS who do *not have* an underlying rheumatic disease special blood immune substances ('autoantibodies'). This means that the immune system may contribute to the FMS condition. Interestingly, around

25% of patients with rheumatic diseases are also diagnosed with FMS. While rheumatic diseases are well treated with drugs, the widespread pain related to FMS does not often improve upon treatment. This study would help us to understand if the immune abnormalities discovered are also present in patients who *do* have both FMS and a rheumatic disease. Furthermore, this study will help us to understand whether such immune abnormalities are the same or different between three rheumatic diseases: Rheumatoid arthritis (RA), Axial Spondyloarthritis (AS) and Behçet's syndrome (BS).

This study is being conducted to gain a better understanding of the specific immune contribution to FMS in patients who have underlying rheumatic diseases. These results will help us to better inform patients about their condition. In the future these findings may lead to new diagnostic tests for FMS and ultimately better treatment options.

Why have I been invited?

- You have been diagnosed with either Rheumatoid arthritis, Axial Spondyloarthritis or Behçet's Syndrome
- You either **do or do not have Fibromyalgia Syndrome** (if you do not have FMS, you will be part of the comparison group (control group))

We expect to have 150 patients like you in this study, which will be carried out at the Pain Research Institute at Liverpool University.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep. We will ask you to sign a consent form to show that you have agreed to take part. Please be aware this study involves animals.

You are free to withdraw at any time, without giving a reason. This will not affect the standard of any NHS care you may receive. If you wish to receive independent general advice about participating in clinical studies, you can contact the Patient Advise and Liaison Service (PALS) at the Walton Centre, on 0151 556 3090.

What will happen if I decide to take part?

- We will ask you to get in touch with us to **register your interest** – this can be via phone call, email or via postage return of the participant response slip (the contact details are at the end of this leaflet)
- Upon receiving your interest, we will **contact you by phone** to discuss participating and answer any queries. We will then arrange a time convenient for yourself to attend the study centre, the **Pain Research Institute** (Clinical Sciences Building, opposite the Liverpool Walton Centre). In the case you would have to travel to reach the location, we will be happy to organize the journey for you. You may eat and drink as normal.
- You will then be posted a **questionnaire booklet** about your pain, to be completed at home and brought to the appointment at the Pain Research Institute.

What will happen to me during the appointment?

- You will be greeted by a member of the research team and provided with COVID -19 Personal Protective Equipment in line with the most up to date hospital policy.
- You will be able to discuss the study in detail together with the researcher and confirm that you are happy to take part. We will then take your written consent and give you one copy of the consent to keep. Note that, after consent, your medical notes may be looked at by doctors, study nurses and administrators involved in this study.
- You will then be asked some questions around your pain, sleep, mood, medical history and family history.

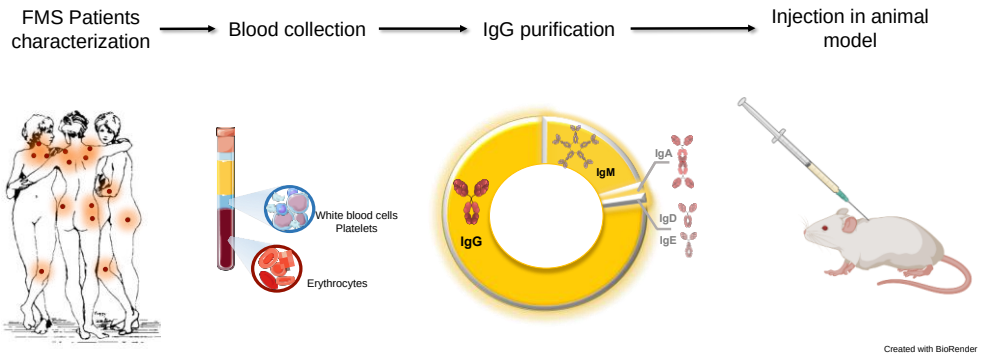
- You will be examined for your rheumatic condition and for fibromyalgia syndrome, which will include applying short-term pressure and a small soft brush over some points of your body. This is used to determine at what pressure you feel pain, termed the “pain pressure threshold”
- We will then assess your eyes using a non-invasive eye imaging technique. We do this in order to examine the small nerve fibres in your eye; such small nerve fibres are sometimes reduced in number in FMS. This will involve, having numbing (anaesthetic) drops and tear drops placed on your eyes then images taken of the front. This takes around 10 minutes.

- Following the eye examination, and if you give your consent for this part of the study, a sample of 120 ml of blood (about 8 tablespoons) will be collected.

Your study visit is then completed. The estimated appointment duration is 90 minutes. You are allowed to drive if you wish. We will reimburse your travel and parking expenses up to a total of £30.00 (please keep receipts where possible). Your participation in this study will not change your medical treatment and no medical treatment will be delayed or withheld.

What will the blood collection be used for?

The autoantibodies (IgG) and other substances purified from your blood sample will be extremely valuable to understand the mechanism of immune abnormalities in patients like yourself with FMS and rheumatic diseases. We will measure and examine these substances in detail. As part of our research we will assess whether their injection to mice causes the painful phenotype, i.e. whether the animals develop a condition similar as fibromyalgia.



What will I commit to do?

We ask you to keep your agreed appointment. If you cannot keep your appointment for any reason, we ask you to tell us about this beforehand, so that we can reschedule to another day. You are free to withdraw from the study at any point. Please inform us of your withdrawal. If you withdraw and you have given serum then your serum will be discarded. However, any blood results from tests already obtained will be used in anonymised form (you cannot be identified).

You will also need to tell us about any problems occurring after the assessment, although such are very unlikely to occur.

What are the risks of taking part?

- *Distress:* Some patients may find answering the questionnaires regarding pain and psychological well-being distressing. If this occurs, please contact us (details at the end) and we can signpost you to support.
- *Inconvenience:* Some patients experience inconvenience when they travel (increased pain from uneven roads, time spent on road).
- *Altered pain:* Patients may experience pain during the short-term examination of pressure of points through their body (a maximum of 20 points) and the brush stroke examination which may linger for a few hours or even days afterwards.
- *Risk of blood taking (venepuncture*)- this is the same procedure you may have had for a blood test at the GP or in clinic.
    - *Infection at blood sampling site* – this risk will be reduced by cleaning the skin prior to the procedure, wearing gloves and using sterile and single -use blood taking equipment
    - *Short-lived pain/ discomfort* - during needle insertion for blood sample obtainment
    - *Haematoma (bruise)* – this risk will be reduced by using the correct blood sampling technique and by applying pressure to the site post procedure

- *Extensive bleeding* – we will identify if you take any medications which increase bleeding prior to the procedure and take precautions accordingly. Also a small gauge needle will be used to minimise risk of bleeding.
- *Vasovagal reaction* (faint) – we will ensure you are adequately hydrated prior to procedure. We will have the ability to lie you flat if you feel faint.
- *Allergic reaction* to cleaning wipes or plasters/latex – we will confirm allergies prior to procedure.
- *Failure to obtain sample* – If we are unable to obtain a sample on the first attempt, two further attempts shall be made. If we remain unsuccessful, no further attempts will be made. You can also withdraw consent for further attempts at any point.

What happens after the appointment?

You are not required to complete any further documentation or attend any further appointments. All continued care will be provided by your existing rheumatological teams. However, you are invited to call the Chief Investigator – Dr Andreas Goebel should you experience anything untoward as time goes by, although this is very unlikely to occur.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the research team, who will do their best to answer your questions (contact numbers are provided at the end of this document). If you remain unhappy and wish to complain formally, you can do this through the University Complaints Procedure. The contact number for Karen Wilding, the responsible officer at the University of Liverpool is 0151 795 1780.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for

legal action for compensation against the University of Liverpool but you may have to pay your legal costs.

Will my information be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential and any information about you, which leaves the immediate research environment, will have your name and address removed so that you cannot be recognised.

Data Protection

Liverpool University is the sponsor for this United Kingdom based study and will act as data controller for this study as such. The research team will be using information from you and your medical records in order to undertake this study. This means that we are responsible for looking after your information and using it properly. Liverpool University will keep identifiable information about you for 30 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. You can find out more about how we use your information by contacting the Chief Investigator, Dr. Andreas Goebel (andreas.goebel@liverpool.ac.uk) or from URL: https://www.liverpool.ac.uk/library/research-data-management/.

The Pain Research Institute will use your name, NHS number, date of birth and contact details to contact you about the research study if necessary, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from Liverpool University and regulatory organizations may look at your medical and research records to check the

accuracy of the research study. The Pain Research Institute will pass these details to Liverpool University along with the information collected from you and your medical records. The only people in Liverpool University who will have access to information that identifies you will be people who need to contact you to for any safety follow up, to invite you to participate in further fibromyalgia or rheumatic disease research over the next five years, or audit the data collection process.

When you agree to take part in a research study, the information about your health and care – without any link to your personal data - may be provided to researchers running other research studies, both in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Moreover, blood samples collected during your appointment will be stored for up to 30 years and could be sent to be examined by laboratories within the UK or abroad. These samples could be used to perform experiments in animal or cellular models in research studies. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research, and it will not be possible for you to be identified by these researchers.

The researchers who analyse the study information will not be able to identify you. This information will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in

a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

Our Liverpool University Data Protection Officer is Mr. Daniel Howarth (0151 794 2148) and you can contact him at: Daniel.Howarth@liverpool.ac.uk.

What will happen to the results of the research study?

Results will be published in relevant medical journals but you will not be identified in any report/publication. You can request a copy of the main outcome from 1.5 years after the end of the study, or if not yet available then, that they can have an abstract summarising results at that time.

Who is organising and funding the research?

The research is being organised by Dr Andreas Goebel, a Pain Medicine Consultant at the Walton Centre, who has expertise in treating patients with chronic pain and by scientists at Kings College London University who are interested in the immune systems role in pain.

The funding comes from the Medical Research Council (MRC); funders have no further say in the conduct of this study.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a 'Research Ethics Committee' to protect your safety, rights, well-being and dignity. This study has been reviewed and given favorable opinion by Wales REC 2 Ethics Committee.

Thank you for taking the time to read about this study.

Participant response

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You can register interest via telephone, email or by postage of the response slip.

To respond via telephone: Please contact the FARR Study Team on 0775545402 to register your interest.

To respond via email:
Email farrstudy@liverpool.ac.uk, including your name, contact details and whether you are interested in participating.

To respond via post: Please send the below response slip to

FARR Study Team
Pain Research Institute, Lower Lane
Liverpool, United Kingdom, L9 7AL

Name……
Contact Number
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Email
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I am interested in taking part in the FARR study (Fibromyalgia and Refractory Pain in Rheumatic diseases) ☐

I am not interested in taking part in the FARR study (Fibromyalgia and Refractory Pain in Rheumatic diseases) ☐

(the best method of contact is: ----------)