NHS
Nottingham
University Hospitals

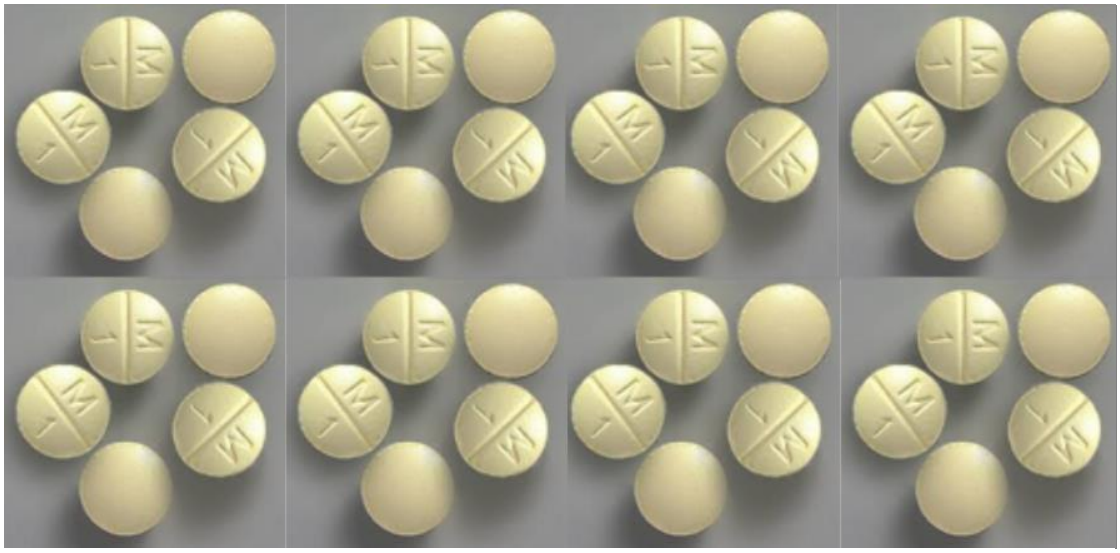
Evaluation of the role of AST/ALT ratio, ELF markers and Fibroscan in the detection of methotrexate-induced hepatotoxicity

For participants aged 16 and over

IRAS Reference: 131770

Participant Information Sheet; Version 8.1, Dated 22-FEB-2024

Principal Investigator: Prof Guruprasad Aithal



Investigator xxxxx

Name:

Contact: Phone and/or email

Researcher:

Name:

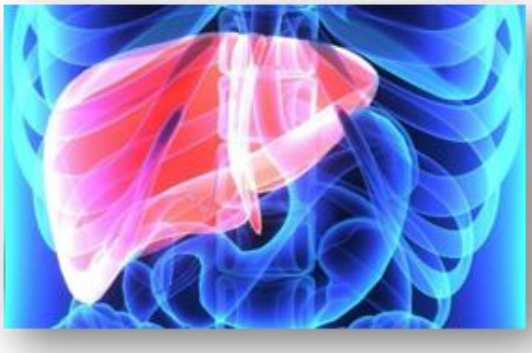
Contact: Phone and/or email

Research & Innovation

1. What is the purpose of the study?

Methotrexate is an anti-rheumatic drug widely used to treat rheumatoid arthritis and psoriasis for more than 50 years. However, there is evidence to suggest that long term use of methotrexate may lead to liver injury and scarring in some patients.

Various guidelines have therefore been developed for doctors to monitor liver health in patients taking methotrexate.



A liver biopsy is recommended to assess the liver but this is not ideal and new non-invasive tests have now become available – e.g. Fibroscan or blood tests such as enhanced liver fibrosis (ELF) test.

It is not yet clear how many patients taking methotrexate develop liver problems or whether the non-invasive monitoring is reliable.

Our goal is to develop the best diagnostic testing programme to ensure liver health is closely monitored in patients taking methotrexate by investigating the effectiveness of various non-invasive tests in the detection of liver scarring in patients with rheumatoid arthritis or psoriasis who are currently on methotrexate. We will also evaluate how genetic variations between people affects their susceptibility to liver scarring.

We aim to include 1200 patients with rheumatoid arthritis or psoriasis, recruited at centres in the UK.

We will not be testing any drugs, treatments or procedures. Taking part will not affect your healthcare in any way. We will offer you a liver fibroscan (similar to ultrasound scan), if you have not previously had one, and take a blood sample for analysis. We will take measurements of your height, weight, and waist and ask about you family and health background.

2. Who has reviewed this study?

Research in the NHS is usually looked at by an independent group called a Research Ethics Committee, to protect your safety, rights, well-being and dignity. This study has been reviewed and given a favourable opinion by the NHS, 'Nottingham 1' Research Ethics Committee.

The study has also been reviewed and approved by the Health Research Authority and the Research & Innovation department of Nottingham University Hospitals NHS Trust. The Nottingham University

Hospitals NHS Trust will act as the 'Sponsor' (i.e., the lead NHS hospital) for this research. The NIHR Nottingham Biomedical Research Centre will fund this research.

3. Why have I been asked to take part?

We are inviting people who have been diagnosed with having psoriasis or rheumatoid arthritis for more than 2 years to take part. We want to include people who have been on methotrexate therapy for the past 6 months or more and people who have never taken methotrexate.

Do I have to take part in this study?

No. It is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form to confirm that you understand what is involved when taking part in this study. If you decide to take part, you are free to leave the study at any time and without giving a reason.

If you withdraw, we will still keep records relating to the treatment given to you, as this is valuable to the study. A decision to withdraw at any time, or a decision not to take part, will not affect the quality of care you receive.

4. What do I have to do?

Participation involves one appointment with our Research Team.

Our Researcher will arrange to meet you at the research centre located in xxxxx, or in the mobile research unit or alternatively arrange to attend your routine hospital clinic appointment and conduct your study visit there.

If you decide to take part, you will be asked to sign a consent form at your appointment. Consent can also be taken verbally (over the telephone) or electronically in conjunction with a phone call, in advance of your appointment which will reduce the amount of time needed for your appointment.

The research team will:

- **try to answer any questions you have,**
- **ask about your health and medical history (including medications),**
- **ask if we can access your Digital health records to collect further details of your health conditions and treatments,**
- **measure your height, weight and waist.**
- **ask you to have a Fibroscan if you have not had a one recently (this is optional- you can indicate this on the consent form). The researcher will upload the results of your Fibroscan to your hospital records and/or Digital Health Record (DHR) which may be accessed by your care team or GP.**

A Fibroscan is a painless ultrasound-like scan that gives information about liver stiffness and liver fat. Liver stiffness can indicate liver fibrosis. A high CAP value can indicate excess liver fat = steatotic liver disease.

To get accurate readings, we recommend that you don't eat for 4 hours before your Fibroscan, and don't drink for 2 hours before the scan. Alcohol should be avoided for 24 hours before the Fibroscan. You should take all your usual medications.

If you are unable to fast due to medical reasons please contact us for advice.

Patients who are/may be pregnant or who have medical implants should not have a Fibroscan.

It is advisable to wear a loose top so your rib area can be accessed for the scan.

- **ask if you are willing to donate any surplus samples left over from your diagnostic tests (such as biopsy tissue), for research (this is optional- you can indicate this on the consent form).**
- **ask if you are willing to allow other researchers to utilise any samples left over after this study finishes by sharing them in a tissue bank. (this is optional- you can indicate this on the consent form)**
- **ask if we can keep your contact details in our database to contact you about study findings and future projects (this is optional- you can indicate this on the consent form).**

If you do decide to take part in the study, you can report any problems you have to your study researcher or doctor. There is more information on this in section 6. There is also a contact number

given at the end of this information sheet for you to phone if you become worried at any time. In the unlikely event of an emergency occurring during the conduct of the study, we may contact your nominated next of kin.

5. What are the possible benefits?

There is no direct benefit to you by taking part in the study, although you may find it useful to have a Fibroscan to check your liver if you have not had one before. The research to evaluate liver scarring tests may lead to improved diagnosis and monitoring of patients like yourself in the future. We do not offer any payment to you for participating but we will try to minimize any inconvenience by arranging an appointment which follows your usual medical/clinic visit.

6. What are the disadvantages?

Having your blood taken may result in some discomfort and slight bruising to your arm. The Fibroscan is routinely used in health centres but can feel uncomfortable and you may feel a sensation patients describe as a 'tickle'. It is not advisable to have a Fibroscan if you are, or may be, pregnant. There are no other risks with this procedure.

7. What will happen to my data?

Will my taking part in this study be kept confidential?

All the information about your participation in this study will be kept confidential. We will keep all information about you safe and secure.

If you consent to take part in this study, the records obtained while you are in this study as well as related health records will remain strictly confidential at all times. The information will be held securely on paper, and electronically at your treating hospital and the main hospital site managing this research under the provisions of the General Data Protection Regulation and the Data Protection Act. Your name will not be passed to anyone else outside the research team or the sponsor, who is not involved in the trial. You will be allocated a trial number, which will be used as a code to identify you on all trial forms.

If you withdraw consent from further study treatment, your data and samples will remain on file and will be included in the final study analysis.

In line with Good Clinical Practice guidelines, at the end of the study, your data will be securely archived for a minimum of 5 years. Arrangements for confidential destruction will then be made.

Informing your General Practitioner (GP) or other healthcare professionals

If you consent, your participation in this research study will be documented in your medical records in the usual ways, based on current hospital policies. The results of the Fibroscan will be uploaded where possible so it can be accessed by the care team at the hospital if required. This information may also be accessible to your GP if viewing is available through electronic record systems (e.g. Digital Health Records in England). All will have a duty of confidentiality to you as a research participant.

We will need to use information from you and your medical records for this research project. This information will include your initials / NHS number / name / contact details / hospital number held by the site for the research. 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.

Some of your information may be sent to academic or commercial institutions abroad for specialist analysis through research collaborations in the future. 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. Sharing of anonymised data following publication allows open scrutiny of our work.

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. If you choose to stop taking part in the study, we would like to continue collecting information about your health from central NHS records and electronic hospital records. If you do not want this to happen, tell us and we will stop.

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 allow the samples and data saved from this study to be used for future research projects. We plan to either store left-over samples in a Human Tissue Authority licensed location or transfer left-over samples to the University of Nottingham

NDDBRU Research Tissue Bank (REC Ref: 19WA0288) when the study ends. The samples and data will be linked using a code.

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
- by emailing the Data Protection Officer for NUH at dpo@nuh.nhs.uk,
- by ringing the Data Protection Officer for NUH on 0115 924 9924 (extension 63975)
- by visiting www.nuh.nhs.uk/gdpr

8. What will happen to the samples I give?

We will measure various substances and constituents of your blood (e.g. proteins, DNA, and fats) in the samples collected for research.

As part of this project or future projects, we may send samples to research teams at other institutions (within or outside the UK) for collaborative health research, or to commercial service providers for specialist analysis. All samples will be labelled with a code so you cannot be identified. All sample shipments and any data sharing for research will require contract agreements with the lead investigator and the research sponsor.

We will assess your blood samples for common genetic (DNA) patterns and variations which relate to drug transport and processing, inflammation, liver injury and scarring of the liver. We will not carry out genetic testing of your samples to detect known inherited disorders. The results of the analysis will not be available to you since this information does not meet quality-control levels required for clinical diagnostics (so may be inaccurate) and the implications of any findings are not currently clear. You can indicate on the consent form if a DNA sample can be collected.

The samples will be securely transported and stored at the study sites/centres. We would like to store any un-used samples left over when the research project has ended for future research studies by us or by researchers (in partnership with us) at other trusted institutions. You will need to indicate on your consent form if you would like your samples to be stored or not.

Only the designated investigator will retain the link between the study code and identifiable information at the study centre. Samples shared outside the institution once the study ends will be fully anonymized. Datasets will be anonymized when shared.

Samples will be destroyed when the study ends if you have not consented for future use and when they are unsuitable for storage. Samples used by other researchers will be returned or destroyed.

9. What happens if new information becomes available?

Sometimes during the course of a research study, new information relevant to your care or treatment becomes available. If this happens, we will tell you about it and discuss with you. If the study is stopped for any reason, there will not be any impact on your medical care.

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

You can decide to withdraw from the study at any time without giving a reason. This will not affect the care you receive. We may not be able to retrieve/remove all your donated samples and data afterwards as they may already be used. We can destroy any samples stored if you ask us to. We would like to use the data we have collected from you but if you request the study data to be withdrawn from analysis we can remove your data from the study database.

11. What happens when the study is finished?

We will publish our findings in research journals and explain them at scientific meetings.

We will provide a summary of our findings on our website:

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This project has already enabled us to make some important observations and identify potential new blood tests. Our achievements are described on our website (http://tinyurl.com/2p83sucz).

A written summary of the research will also be available from the research team. If you consent to storage of your contact details, we will send you the summary.

12. What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your question.
FOR PATIENTS IN ENGLAND: If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital or you can contact the Patient Advice and Liaison Service (PALS) telephone 0800 183 0204.
In the event that something does go wrong and you are harmed during the research study there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you may have grounds for a legal action for compensation but you may have to pay your legal costs. The normal NHS complaints mechanisms will still be available to you.

13. Further Information

You are encouraged to ask any questions you wish before, during or after your treatment. If you have any questions about the study please speak to the research team who will be able to provide you with up to date information about the study. If you require any further information or have any concerns while taking part in the study please contact your study team or lead doctor (both are listed at the top of this document).

If you decide you would like to take part then please read and sign the consent form. You will be given a copy of this information sheet and the consent form to keep. A copy of the consent form will be filed in your medical notes (if applicable), and one will be filed with the study records.

Patient and Public Involvement

All research participants should be offered the opportunity to feedback on their experiences of taking part in clinical research at NUH through the Participant in Research Excellence Survey (PRES). PRES is a

requirement for all NIHR-adopted studies (although participants are free to choose if they want to participate or not).

The web link is: *www.nuh.nhs.uk/ri-feedback*

We also need volunteers to be members of our Patient & Public Advisory Group To:

- Comment on our research ideas;
- Comment on how research studies should be done;
- Assist us in recruiting people to our clinical trials
- Provide us with your thoughts on how we can better communicate our work

For more information ask or contact: XXXXXXX

Our website: xxxx

If you would like to take part, please contact us at the address below:

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You can have more time to think this over if you are at all unsure.

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