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Stratify methotrexate: a study to investigate the liver function of patients taking methotrexate, and risk-stratify them accordingly

Submission date
28/10/2019

Recruitment status
Suspended

Registration date
18/11/2019

Overall study status
Completed

Last Edited
14/07/2020

Condition category
Digestive System

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Methotrexate is a drug widely prescribed, however the most appropriate method of monitoring is debated and currently unclear, demonstrated by divergent guidelines across specialities. Historically concerns have been raised regarding methotrexate and the development of liver fibrosis; more recent publications have cast doubt upon this potential relationship.

The discovery of novel, non-invasive methods to assess liver fibrosis, such as transient elastography (e.g. FibroScan®) have allowed fresh consideration into this difficult area.

This study aims to assess the prevalence of liver fibrosis (by way of FibroScan®, blood tests and clinician review) in participants who are taking methotrexate, compared with those who have never taken this drug.

Who can participate?
Patients aged over 18 who are have been taking methotrexate for six months or more, and age matched controls who have never taken methotrexate

What does the study involve?
Risk factors for liver fibrosis will be assessed for each participant e.g. presence of diabetes mellitus, BMI and body mass composition, current and previous alcohol use, cumulative dose and duration of methotrexate use etc.

What are the possible benefits and risks of participating?
Possible benefits of taking part in this research include the health checks included as part of it, which you are informed at the time. For the majority of people, these health checks are very reassuring. Should any abnormalities be found then referral for appropriate assessment and investigations will be undertaken.
The culmination of this research should better inform clinicians about risk factors for potential liver injury in those individuals taking methotrexate, and help to shape future guidelines.
There is a possibility that the health checks performed show up a problem. In this circumstance,

patients would be informed immediately and the next appropriate steps will be organised and made clear. We appreciate the discovery of health-related findings can cause worry and the staff are on hand to discuss any concerns

Where is the study run from?
York Hospital (UK)

When is the study starting and how long is it expected to run for?
From June 2019 to December 2021 (updated 14/07/2020, previously: September 2020)

Who is funding the study?
LIVErNORTH (UK)

Who is the main contact?
Dr Lucy Turner, lucy.turner7@nhs.net
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Contact information

Type(s)
Scientific

Contact name
Dr Lucy Turner

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
42142

Study information

Scientific Title
A study to investigate the liver function of patients taking methotrexate, and risk-stratify them accordingly

Study objectives
There is no difference in the prevalence of liver fibrosis between individuals taking methotrexate, compared with those who are not

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 18/06/2019, NHS HRA (Health Research Authority, Skipton House, 80 London Road, London, SE1 6LH), ref: 19/NE/0176

Study design
Non-randomized; Observational; Design type: Validation of investigation /therapeutic procedures

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Liver fibrosis

Interventions
Participants will be recruited largely from rheumatology and dermatology outpatient clinics in York and Scarborough Hospitals. Over the 12 month study period we will aim to recruit 698 patients. Controls will be matched by age and gender. Risk factors for liver fibrosis will be assessed for each participant e.g. presence of diabetes mellitus, BMI and body mass composition, current and previous alcohol use, cumulative dose and duration of methotrexate use etc.

The following things will be undertaken for each study participant:
a) Electronic record
The PI will evaluate historical data from the patient electronic record; including blood test results, duration and cumulative dose of MTX prescribed (if relevant), patient demographic data such as postcode, age and gender. The data will be recorded in an EXCEL file, with no patient

identifiable factors. All information will be kept on an encrypted password protected York NHS Trust IT system.
b) Participant questionnaire
Participants will be asked to complete a lifestyle questionnaire. This will be anonymous; they will be given adequate time and assisted for any special needs as appropriate. The questionnaire focusses on patients' understanding and knowledge of methotrexate. The answers are in both qualitative and quantitative fashion. Answers will be compiled, cumulated and analysed.
c) Participant history and special tests
This part of the study will be largely completed by the PI. Participants will be reviewed in an outpatient environment. Participants will receive an Invite Letter and Participant Information Sheet through the post. Participants can either contact the research team in advance to make a mutually agreeable time to meet, or they can meet a member of the research team on the day of their existing outpatient appointment. The research member conducting the review will go through the questions detailed in the proforma. These questions are based on the participants' medical history, medications and alcohol intake - both historical and current. The research team member will go on to perform a liver Fibroscan® and body mass composite score. If blood tests have not been performed for the last three months, then the research member will request bloods (in keeping with current guidance). This information will be recorded onto an anonymised sheet.

Following the interview these sheets will be manually inserted onto a larger, anonymised database, also kept on an encrypted password-protected York NHS Trust IT system linked computer. When inserting the individuals' dataset onto the spreadsheet the information will be coded, for the ease of data analysis.

A patient group was involved in the compilation of the research methodology. Following their feedback alteration was undertaken to the consent form, participant information leaflet, invite letter, questionnaire, and posters for the research study.

The proposed sample size for this project is a total of 698 participants - 349 in each arm. This power calculation was calculated using existing data suggesting that the prevalence of liver fibrosis in patients taking methotrexate is reported as 5%, and the prevalence of liver fibrosis in patients not taking methotrexate as 1.3% in the UK population. This study uses a case control ratio of 1:1 and assumes a power of 80%.

Participant Journey:
From a participant point of view the following summarises their proposed progress through the study:
1) Receipt of a Participant Information Sheet and Invite Letter for study, with their pre-existing planned outpatient appointment.
2) Immediately after attendance at there planned outpatient appointment, they will have the opportunity to be recruited into the study which includes the following:
- Consent process
- Lifestyle questionnaire
- Medical history questions
- FibroScan®
- Body mass composition measurement
This will take approximately 30 minutes. Following this the participants' involvement in the study is complete. No additional visits or follow-up is required

Intervention Type
Other

Primary outcome measure
Presence of liver fibrosis (by liver Fibroscan®)

Secondary outcome measures
Risk factors for liver fibrosis will be assessed for each participant e.g. presence of diabetes mellitus, BMI and body mass composition, current and previous alcohol use, cumulative dose and duration of methotrexate use etc.

Overall study start date
03/09/2018

Completion date
31/12/2021

Eligibility

Key inclusion criteria
1. Individuals in the methotrexate cohort must have taken this medication for at least 6 months
2. All participants must be over 18 years old

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 2,000; UK Sample Size:2,000

Key exclusion criteria
1. Pregnant females
2. Previously taken methotrexate, but are no longer currently taking it
3. Lack capacity to consent

Date of first enrolment
25/06/2019

Date of final enrolment
31/12/2021

Locations

Countries of recruitment

England

United Kingdom

Study participating centre
York Hospital
Wigginton Road
York
United Kingdom
YO31 8HE

Sponsor information

Organisation
York Teaching Hospital NHS Foundation Trust

Sponsor details
York Hospital
Wigginton Road
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+44 (0)1904725123
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/027e4g787

Funder(s)

Funder type
Charity

Funder Name
LIVErNORTH

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
31/12/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.
Name: Lucy Turner
Email: lucy.turner7@nhs.net
Consent from participants was obtained for this sharing of data
All data will be completely anonymised
Data will be available from completion of study (25/06/20) for 1 year
Type of data:
1. Participant age
2. Height
3. Weight
4. BMI
5. Ethnicity
6. Gender
7. MTX cumulative dose (if appropriate)
8. other mediations
9. comorbidities
10. FibroScan result
11. Alcohol consumption (units per week)
12. Audit C score

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No