

Vaccine Response On/off Methotrexate (VROOM): does temporarily suspending methotrexate treatment for two weeks enhance COVID-19 vaccine response?

Submission date 22/07/2021	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 23/08/2021	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 25/01/2024	Condition category Musculoskeletal Diseases	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

The purpose of the VROOM study is to find out if an individual's response to a vaccine can be improved. Specifically the VROOM study will aim to recruit individuals who have inflammatory conditions such as rheumatoid arthritis and psoriasis and routinely take a drug called methotrexate. The individuals needed for the study are these individuals and specifically those who are invited to and accept an invitation to have a booster vaccination against COVID-19 from the NHS vaccination programme.

Doctors and scientists believe there is a small amount of evidence that if individuals temporarily stop taking their methotrexate for the two weeks around when they receive their COVID-19 booster- it may improve their body's (immune) response. The study will also help understand the way in which methotrexate dampens the immune response to vaccines.

Methotrexate is the first-line treatment for inflammatory conditions such as rheumatoid arthritis and psoriasis. It does a good job at controlling such diseases but it also reduces the body's ability to fight infections. People taking methotrexate also don't get great responses to vaccines such as those against the flu and pneumonia. Better immunity usually means a better chance of not getting infected and fighting the virus if infected. Because there is no clear evidence on whether to halt or continue methotrexate during COVID-19 vaccinations, specialists have given conflicting advice that has confused patients. There is an opportunity to answer this question during the booster vaccinations in winter 2021.

Who can participate?

We will invite 560 people with inflammatory conditions such as rheumatoid arthritis and psoriasis receiving methotrexate to take part in our study looking at vaccine response in those who continue to take their methotrexate as usual or who take a 2-week break from taking their methotrexate around their COVID-19 booster vaccination.

What does the study involve?

Participants will be invited to 3 hospital visits to give some data and a small blood sample at each visit.

What are the possible benefits and risks of participating?

We hope that the valuable information from this study will give the NHS and other countries a clear answer to the question of whether temporarily stopping methotrexate for 2 weeks around the time of COVID-19 booster vaccination improves the vaccine response. We cannot promise that the study will benefit those that participate directly, but the information generated has the potential to benefit all those with inflammatory conditions who continue to be vaccinated against COVID-19 in the future. Thus, the results of this study may benefit those that participate in the future.

There is a small risk of a flare in a participant's inflammatory condition on interrupting methotrexate treatment for two weeks. However, all participants can access treatment for any flare-ups as usual.

Where is the study run from?

The study is sponsored by the University of Nottingham (UK) and runs from the Oxford Clinical Trials Research Unit (OCTRU), a UKCRC-registered CTU.

When is the study starting and how long is it expected to run for?

From July 2021 to September 2022

Who is funding the study?

National Institute for Health Research (NIHR) Efficacy and Mechanism Evaluation Programme (UK)

Who is the main contact?

VROOM study team
vroom@ndorms.ox.ac.uk

Contact information

Type(s)

Public

Contact name

Dr Jennifer Williams

Contact details

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Type(s)

Scientific

Contact name

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

CPMS 50297, v1.0

Study information

Scientific Title

A multi-centre randomised controlled trial examining the effects of temporarily suspending low-dose methotrexate treatment for two weeks after SARS-CoV-2 vaccine booster on vaccine response in immunosuppressed adults with inflammatory conditions, including a nested mechanistic sub-study

Acronym

VROOM

Study objectives

A two-week temporary suspension in weekly low-dose methotrexate treatment after SARS-CoV-2 vaccine boosters will improve the anti-spike-receptor binding domain (RBD) response.

Mechanistic sub-study (in a subset of 100 participants):

The neutralising antibody response will correlate with the anti-spike-RBD antibody in this immune-suppressed population as in other healthy populations.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 20/08/2021, Yorkshire & The Humber - Leeds West Research Ethics Committee (Meeting held by video-conference via Zoom; +44 (0)207 972 2504, +44 (0)207 104 8088; leedswest.rec@hra.nhs.uk), ref: 21/YH/0209

Study design

Multi-centre interventional randomized controlled trial

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Inflammatory polyarthropathies, rheumatoid arthritis, psoriasis, seronegative spondyloarthritis, reactive arthritis, atopic eczema, polymyalgia rheumatica, systemic lupus erythematosus

Interventions

Participants will be randomised into the two arms (experimental intervention or control intervention) in a 1:1 ratio using the minimisation factors:

1. Inflammatory condition type (inflammatory rheumatic disease (+/- skin disease), skin disease alone)
2. Age group (<40 years, 40-64 years, ≥65 years)
3. Previous vaccination platform received (mRNA, vector, combination)

Allocation will occur using a bespoke randomisation system developed and validated within the Oxford Clinical Trials Research Unit (OCTRU) at the University of Oxford. Participants will enter their age group, inflammatory condition grouping, and which 2 COVID vaccinations were received previously into the randomisation system.

Experimental intervention: To suspend methotrexate for two weeks immediately after receiving the SARS-CoV-2 booster vaccination.

Control intervention: To continue on the same dose of methotrexate as usual after SARS-CoV-2 booster vaccination.

Intervention Type

Drug

Phase

Phase III/IV

Drug/device/biological/vaccine name(s)

Methotrexate

Primary outcome(s)

Anti-spike receptor binding domain (RBD) antibody level measured from blood sample collected at 4 weeks post SARS-CoV-2 booster vaccination

Key secondary outcome(s)

1. Level of anti-spike RBD antibody measured from blood sample collected at 12 weeks post booster vaccination
2. Patient assessments of disease activity measured using:
 - 2.1. Global assessment using a numeric rating scale with one-week recall at baseline, 2, 4, and 12 weeks post booster vaccination
 - 2.2. Current disease activity level and change since booster, 4 and 12 weeks post booster vaccination
3. Disease flare-up and actions taken to deal with them measured using patient self-report at 4 and 12 weeks post booster vaccination
4. Effect on quality of life measured using the EQ-5D-5L questionnaire at 4 and 12 weeks post booster vaccination
5. Adherence with advice to interrupt or continue methotrexate measured using patient self-report at 2 and 4 weeks post booster vaccination

Mechanistic sub-study only:

1. COVID-19 neutralising titre measured from blood sample collected at 4 and 12 weeks post booster vaccination
2. Adherence to methotrexate allocation measured using patient self-report at 4 and 12 weeks post booster vaccination

Completion date

26/09/2022

Eligibility

Key inclusion criteria

1. Aged ≥ 18 years
2. Diagnosed with inflammatory conditions such as rheumatoid arthritis, psoriasis with or without arthritis, seronegative spondyloarthritis, reactive arthritis, atopic eczema, polymyalgia rheumatica, or systemic lupus erythematosus. This is not an exhaustive list and people with other inflammatory conditions where treatment may be interrupted for two weeks without the risk of a substantial increase in disease activity, or organ or life-threatening flare up will also be eligible to participate in the study in order to increase the generalisability of the study.
3. Prescribed with oral or subcutaneous methotrexate (≤ 25 mg/week) +/- hydroxychloroquine weekly administered for at least the previous three months
4. Able to temporarily suspend methotrexate for two weeks in the opinion of patients' consultant without the risk of substantial increase in disease activity, or organ or life-threatening flare-up
5. Able to give informed consent;
6. Eligible for planned booster vaccination for COVID-19 (i.e. have received any 2 vaccinations from the original NHS COVID Vaccination Programme 2020/21)

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Total final enrolment

383

Key exclusion criteria

Current participant exclusion criteria as of 08/03/2022:

1. Diagnosed with any of: ANCA associated vasculitis, large vessel vasculitis, myositis, giant cell arteritis, solid organ transplant or any another inflammatory condition for which treatment cannot be interrupted safely.
2. Treated with Rituximab drip in the last 18 months or planning to start it
3. Concurrent immune suppressive treatments in the last two months specifically leflunomide, ciclosporin, azathioprine or mercaptopurine, sulfasalazine or other 5-amino-salicylic acid drugs, mycophenolate, apremilast, or biologic agents
4. Radiotherapy or cancer chemotherapy in last six months
5. Prednisolone dose >7.5 mg/day within 30 days of randomisation
6. Active solid organ cancer (people with skin cancer or those cured of solid organ cancer are eligible)

Previous participant exclusion criteria:

1. Diagnosed with inflammatory conditions for which treatment cannot be interrupted safely such as ANCA associated vasculitis, large vessel vasculitis, myositis, giant cell arteritis, or solid organ transplant
2. Treated with Rituximab drip in the last 18 months or planning to start it
3. Concurrent immune suppressive treatments in the last two months specifically leflunomide, ciclosporin, azathioprine or mercaptopurine, sulfasalazine or other 5-amino-salicylic acid drugs, mycophenolate, apremilast, or biologic agents
4. Radiotherapy or cancer chemotherapy in last six months
5. Prednisolone dose >7.5 mg/day within 30 days of randomisation
6. Active solid organ cancer (people with skin cancer or those cured of solid organ cancer are eligible)

Date of first enrolment

30/09/2021

Date of final enrolment

07/03/2022

Locations

Countries of recruitment

United Kingdom

England

Wales

Study participating centre

Nottingham University Hospitals NHS Trust

Trust Headquarters
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre

Sherwood Forest Hospitals NHS Foundation Trust

Kings Mill Hospital
Mansfield Road
Sutton-in-ashfield
United Kingdom
NG17 4JL

Study participating centre

Royal Wolverhampton NHS Trust

Clinical Trials Unit
Cannock Chase Hospital
Brunswick Road
Cannock
Staffordshire
United Kingdom
WS11 5XY

Study participating centre

Great Western Hospitals NHS Foundation Trust

Great Western Hospital
Marlborough Road
Swindon
United Kingdom
SN3 6BB

Study participating centre

Aneurin Bevan University Health Board

Royal Gwent Hospital
Cardiff Road

Newport
United Kingdom
NP20 2EF

Study participating centre

Chesterfield Royal Hospital NHS Foundation Trust
Chesterfield Road
Calow
Chesterfield
United Kingdom
S44 5BL

Study participating centre

Cwm Taf Morgannwg University Local Health Board
Royal Glamorgan Hospital
Ansari Court
United Kingdom
CF72 8TB

Study participating centre

Gateshead Health NHS Foundation Trust
Queen Elizabeth Hospital
Sheriff Hill
Gateshead
United Kingdom
NE9 6SX

Study participating centre

Harrogate and District NHS Foundation Trust
Harrogate District Hospital
Lancaster Park Road
Harrogate
United Kingdom
HG2 7SX

Study participating centre

Imperial College Healthcare NHS Trust
Hammersmith Hospital
Du Cane Road

London
United Kingdom
W12 0HS

Study participating centre
Lancashire & South Cumbria NHS Foundation Trust
Royal Preston Hospital
Vicarage Lane
Preston
United Kingdom
PR2 8DW

Study participating centre
Midlands Partnership NHS Foundation Trust
Haywood Hospital
High Lane
Stoke on Trent
United Kingdom
ST6 7AG

Study participating centre
Norfolk and Norwich University Hospitals NHS Foundation Trust
Colney Lane
Colney
Norwich
United Kingdom
NR4 7UY

Study participating centre
North Cumbria Integrated Care NHS Foundation Trust
Clinical Research Department
The Cumberland Infirmary
Port Road
Carlisle
United Kingdom
CA2 7AF

Study participating centre
North West Anglia NHS Foundation Trust
Peterborough City Hospital
Bretton Gate

Bretton
Peterborough
United Kingdom
PE3 9GZ

Study participating centre
Oxford University Hospitals NHS Foundation Trust
Nuffield Orthopaedic Centre
Windmill Road
Oxford
United Kingdom
OX3 7LD

Study participating centre
The Dudley Group NHS Foundation Trust
Russells Hall Hospital
Pensnett Road
Dudley
United Kingdom
DY1 2HQ

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
The Queen Elizabeth Hospital
Gayton Road
King's Lynn
United Kingdom
PE30 4ET

Study participating centre
The Robert Jones and Agnes Hunt Orthopaedic Hospital NHS Foundation Trust
Gobowen
Oswestry

United Kingdom
SY10 7AG

Study participating centre

Torbay and South Devon NHS Foundation Trust

Torbay Hospital
Newton Road
Torquay
United Kingdom
TQ2 7AA

Study participating centre

University Hospital Southampton NHS Foundation Trust

Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre

University Hospitals Coventry and Warwickshire NHS Trust

University Hospital of Coventry and Warwickshire
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Study participating centre

University Hospitals Sussex NHS Foundation Trust

Royal Sussex County Hospital
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Brighton
United Kingdom
BN2 1ES

Study participating centre

Wirral University Teaching Hospital NHS Foundation Trust

Arrowe Park Hospital
Arrowe Park Road
Upton
Wirral

United Kingdom
CH49 5PE

Study participating centre

York and Scarborough Teaching Hospitals NHS Foundation Trust

York Hospital
Wigginton Road
York
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YO31 8HE

Sponsor information

Organisation

CTU0373

ROR

<https://ror.org/01ee9ar58>

Funder(s)

Funder type

Government

Funder Name

Efficacy and Mechanism Evaluation Programme

Alternative Name(s)

NIHR Efficacy and Mechanism Evaluation Programme, Efficacy and Mechanism Evaluation (EME),
EME

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

Participant level dataset and statistical code will be made available upon reasonable request to OCTRU and the CI, once the VROOM study findings have been published in full. Some specific data items may not be shared in order to maintain participant anonymity.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		27/06/2022	01/07/2022	Yes	No
Results article		12/12/2023	25/01/2024	Yes	No
Protocol article		03/05/2022	04/05/2022	Yes	No
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes