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The Monoclonal Antibody Medications in inflammatory Arthritis: stopping or continuing in pregnancy (MAMA) trial

Submission date
01/08/2024

Recruitment status
Recruiting

Registration date
23/10/2024

Overall study status
Ongoing

Last Edited
27/05/2025

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
1-2% of women are affected by inflammatory arthritis. Many are treated with medications known as ‘biologics’. More women with inflammatory arthritis are considering starting a family, because biologics mean they are more able to manage their arthritis. They may face difficult decisions around treatments during pregnancy. Uncontrolled arthritis can lead to worse outcomes in pregnancy, so managing arthritis well is important. Biologics are often avoided during pregnancy because of limited understanding of how these drugs impact pregnancy or arthritis activity. There are concerns about the possible effects of these drugs on babies’ immune systems, and some baby vaccinations are routinely delayed. Until recently, most women were advised to stop their biologics during pregnancy; however, due to mounting evidence of their safety, national guidance now states that women can stay on biologics throughout pregnancy. It is unknown whether there is any benefit to this in terms of arthritis control. Certain other medicines used to treat arthritis flares in pregnancy can pose potential harm. MAMA aims to find out the effects of stopping or continuing biologics during pregnancy. It will compare whether women who continue their biologics have better arthritis control than those who stop, and assess the impact on their pregnancy, their baby, and the costs associated with this decision.

Who can participate?
Pregnant women at less than 28 completed weeks’ gestation, aged 16 years old and over with a diagnosis of rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA) and prescribed a regularly dosed bDMARD

What does the study involve?
Participants will have an equal (random) chance to continue their biologics throughout pregnancy or to stop by the 28 weeks of pregnancy. During pregnancy, women will be asked to complete a simple arthritis symptom severity questionnaire, monthly via an app (or in writing) and at 3, 6 and 12 months after the baby is born. The woman will be asked if they would be happy for their baby to have blood tests to check their immune response to vaccinations. Mums and babies will be followed up until 24 months after the end of pregnancy, their general health and their baby's development.

This is a trial of two treatment strategies relating to continuing or stopping prescribed bDMARDs. bDMARDs are a broad group of drugs which includes many classes and within each class, many marketed products are largely similar in safety profile. The classes of bDMARDs included in this study are detailed in the inclusion criteria and the MAMA trial Reference Safety Information. All drugs are licensed for use in inflammatory arthritis and are already prescribed in pregnancy. Additionally, their use in pregnancy is outlined in the 2022 BSR guidelines on the use of medications in pregnancy.

What are the possible benefits and risks of participating?
Whilst there are no direct benefits to taking part, your contribution may help answer an important question, which could benefit women and their babies in the future.

Both continuing and stopping using bDMARDs beyond 28 weeks of pregnancy are routine practices in the UK so there are no additional risks to being involved in the trial. Stopping biologic medications can increase the risk of disease activity and flares during pregnancy. Continuing biologic medication in pregnancy may have possible effects on babies' immune systems, and some baby vaccinations may be delayed. This will be discussed with women as part of their clinical care they will also be encouraged to discuss any concerns with their rheumatologist or clinical team.

Optional Infant Immunology part of the Trial
Blood sampling can cause bruising or pain, minimised with local anaesthetic cream.

Where is the study run from?
National Perinatal Epidemiology Unit (NPEU), University of Oxford, UK

When is the study starting and how long is it expected to run for?
July 2024 to February 2030

Who is funding the study?
NIHR Health Technology Assessment Programme, HTA

Who is the main contact?
mama@npeu.ox.ac.uk

Study website
https://www.npeu.ox.ac.uk/mama

Contact information

Type(s)
Public, Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1009876

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 65203

Study information

Scientific Title
The Monoclonal Antibody Medications in inflammatory Arthritis: stopping or continuing in pregnancy (MAMA) trial

Acronym
MAMA

Study objectives
Primary objectives:
To compare the peak of disease activity up to 6 months after the end of pregnancy in pregnant women with AIA randomised to continue bDMARDs versus those randomised to stopping bDMARDs before the third trimester of pregnancy.

Secondary objectives:
In pregnant women with AIA randomised to continue bDMARDs versus those randomised to stopping bDMARDs before the third trimester of pregnancy:
To compare the peak of disease activity up to 12 months after the end of pregnancy
To compare other features of arthritis disease activity
To investigate pregnancy outcomes
In infants born to women with AIA randomised to continue bDMARDs versus those randomised to stop bDMARDs
To compare neonatal outcomes
To investigate infant and child outcomes including global development at 24 months of age, infection up to 24 months of age, and immune function at 2, 5 and 13 months (in a subset of infants where consent has been obtained with an address within geographical reach of Oxford)

Economic evaluation:
To examine using an economic evaluation, whether any additional benefits associated with continuing bDMARDs are justified by any additional health care resources needed

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 30/09/2024, London - Central Research Ethics Committee (3rd Floor 3 Piccadilly Place, London Road, Manchester, M1 3BN, United Kingdom; +44 (0)207 104 8061; londoncentral.rec@hra.nhs.uk), ref: 24/LO/0678

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Home, Hospital

Study type(s)
Efficacy

Participant information sheet

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

Health condition(s) or problem(s) studied
Pregnant women less than 28 completed weeks of gestation prescribed a regularly dosed biologic disease-modifying anti-rheumatic drug (bDMARD) for Autoimmune Inflammatory Arthritis (AIA)

Interventions
This trial will compare two existing pathways of care for bDMARD use in pregnancy that are already being used in the UK, albeit with wide variation. MAMA is a pragmatic, comparative effectiveness trial of these two pathways of care.

The two pathways of care being assessed are:
1. Intervention: continuing bDMARDs throughout pregnancy. The woman's current bDMARD, dose and frequency of administration will continue.
2. Comparator: stopping bDMARDs before the third trimester (week 28) of pregnancy and restarting no earlier than 2 weeks after the end of pregnancy.

For both groups, all other aspects of clinical care are determined by the treating clinical team.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacoeconomic, Prophylaxis, Therapy, Others (This is a trial of two treatment strategies relating to continuing or stopping prescribed bDMARDs. The classes of bDMARDs included in this study are detailed in the inclusion criteria and the MAMA trial Reference Safety Information. All drugs are licensed for use in inflammatory arthritis and are already prescribed in pregnancy. Additionally, their use in pregnancy is outlined in the 2022 BSR guidelines on use of medications in pregnancy.)

Phase
Phase III

Drug/device/biological/vaccine name(s)
Humira [adalimumab], Enbrel [etanercept], Remicade [infliximab], Simponi [golimumab], Cimzia [certolizumab pegol], ORENCIA [abatacept], RoActemra [tocilizumab], Kevzara [sarilumab], Kineret [anakinra], Ilaris [canakinumab], Cosentyx [secukinumab], Taltz [ixekizumab], Bimzelx [bimekizumab], Tremfya [guselkumab], Skyrizi [risankizumab], Stelara [ustekinumab]

Primary outcome measure
Peak disease activity measured by the highest RAPID3 total score [self-report] from randomisation up to 6 months after the end of pregnancy

Secondary outcome measures
Measured at variable time points up to 24 months after the end of pregnancy:
1. Peak disease activity measured by the highest RAPID3 total score [self-report]
2. Peak pain level measured by the highest RAPID3 pain score [self-report]
3. Peak overall wellbeing measured by the highest RAPID3 patient global estimate score [self-report]

4. Any occurrence of arthritis flare [self-report]
5. Need for escalation of therapy due to inflammatory disease activity [self-report], defined as:
• New or increased dose of any DMARD for arthritis;
• New or increased dose of systemic glucocorticoid (GC) for arthritis (oral or intramuscular injection);
• Received intra-articular GC joint injection
6. Any use of NSAIDs and frequency of use for treatment of joint pain [self-report] (described only using summary statistics)
7. Any occurrence of arthritis flare [maternal self-report] (described only using summary statistics)
8. Health-related quality of life measured using the EQ-5D-5L
9. Anxiety and depression measured using the EQ-5D-5L
10. Livebirth
11. Stillbirth (fetal loss greater than or equal to 24 weeks' gestation)(described using summary statistics)
12. Pregnancy loss less than 24 weeks' gestation (described using summary statistics)
13. Termination of pregnancy (with or without known congenital anomaly)
14. Mode of birth (described only using summary statistics)
15. Preterm prelabour rupture of membranes (described only using summary statistics)
16. New diagnosis of pre-eclampsia (described only using summary statistics)
17. New diagnosis of gestational diabetes (described only using summary statistics)
18. Venous thromboembolism (described only using summary statistics)
19. Confirmed or suspected maternal infection (defined as positive culture from a usually sterile site and/or maternal treatment with antibiotics) (described only using summary statistics)
20. Gestational age (continuous) and preterm birth at:
- <28
- 28 to <32 and
- 32 to 37 gestational weeks
21. Birth weight z-score
22. Early-onset neonatal infection: (<72 hours after birth), microbiologically-confirmed or clinically suspected infection
23. Late-onset infection (>72 hours after birth): microbiologically-confirmed or clinically suspected infection
24. Neonatal death (up to 24 months)
25. Neonatal unit admission
26. Received intensive care (described only using summary statistics)
27. Necrotising enterocolitis (NEC). [defined as babies born <32+0 gestational weeks where NEC is diagnosed at surgery, post-mortem or based on the following clinical and radiographic signs:
27.1. At least one clinical feature from:
• Bilious gastric aspirate or emesis
• Abdominal distension
• Occult or gross blood in the stool (no fissure)
27.2. And at least one radiographic feature from:
• Pneumatosis
• Hepato-biliary gas
• Pneumoperitoneum] (described only using summary statistics)
28. Brain injury [defined as any of neonatal seizures, intracranial haemorrhage (including intraventricular/periventricular haemorrhage grade 3 or 4), perinatal/neonatal stroke, hypoxic-ischaemic encephalopathy, central nervous system infection, bilirubin encephalopathy and among preterm infants only, cystic periventricular leukomalacia] (described only using summary statistics)
29. Chronic lung disease [defined as babies born <32+0 gestational weeks who are alive and

receiving any respiratory support at 36+0 corrected gestational weeks] (described only using summary statistics)
30. Retinopathy of prematurity requiring treatment [defined as babies born <32+0 gestational weeks who received treatment with laser, cryotherapy or intravitreal injection for retinopathy of prematurity] (described only using summary statistics)
31. Any congenital anomaly [classified according to Eurocat] and to include congenital heart block as recommended by EULAR (described only using summary statistics)

Key long-term outcome:
32. Child development (measured using the parent-completed Ages and Stages Questionnaire-3 (ASQ-3) 24-month questionnaire total score)
33. ASQ-3 score below the cut-off for risk of developmental delay in the following domains:
• Communication skills
• Gross motor skills
• Fine motor skills
• Problem-solving skills
• Personal social skills
(described only using summary statistics)
34. Number of infections (defined by admission to hospital for infection or prescribed antibiotic treatment for infection)
35. Duration of breastfeeding
36. Infant death up to 24 months of age
37. Healthcare utilisation and costs
Including neonatal unit admission level of care: intensive care, high dependency, special care, transitional care, including length of stay at different care levels
38. Quality-adjusted life years (QALYs)
39. Cost-consequence analysis
40. Cost-utility analysis
41. Child Quality of Life (measured using the parent-completed PedsQL)
Infant Immunology subset infants:
42. Child vaccine/immunological response:-
• Total IgG/A/M immunoglobulin levels
• Detailed lymphocyte phenotyping
• Vaccine-specific antibodies (diphtheria, tetanus, pertussis antigens, Hib and measles antibody, and PCV13 at 13 months only)

Overall study start date
30/07/2024

Completion date
28/02/2030

Eligibility

Key inclusion criteria
Current inclusion criteria as of 20/12/2024:

Pregnant women with Autoimmune Inflammatory Arthritis (AIA), satisfying the following criteria:
1. Have a diagnosis of rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA)
2. Pregnant at less than 28 completed weeks' gestation

3. Prescribed a regularly dosed bDMARD (including biologic originators and biosimilars) for RA, JIA, PsA or axSpA.
4. Aged 16 years or over
5. Has provided informed consent

For Infant Immunology (optional element):
6. Address “within geographical reach” from the Oxford Vaccine Group
7. Ongoing consent from parents for infant immunological follow-up

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Previous inclusion criteria:

Pregnant women with Autoimmune Inflammatory Arthritis (AIA), satisfying the following criteria:
1. Have a diagnosis of rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA)
2. Pregnant at less than 28 completed weeks’ gestation
3. Prescribed a regularly dosed bDMARD (including biologic originators and biosimilars) for RA, JIA, PsA or axSpA. This includes all current bDMARDs in the following classes and any future bDMARD licensed under these same classes:
3.1. Biologic drugs which block Tumour necrosis factor (TNF)
3.2. Biologic drugs which block CD80/86
3.3. Biologic drugs which block Interleukin 6
3.4. Biologics which block interleukin 1
3.5. Biologics which block interleukin 17
3.6. Biologics which block interleukin 23
3.7. Biologics which block interleukin 12/23
4. Aged 16 years or over
5. Has provided informed consent

For Infant Immunology (optional element):
6. Address “within geographical reach” from the Oxford Vaccine Group
7. Ongoing consent from parents for infant immunological follow-up

Participant type(s)
Patient

Age group
Mixed

Lower age limit
16 Years

Sex
Female

Target number of participants
328

Key exclusion criteria

1. Prescribed rituximab either during pregnancy or in the 6 months prior to conception
2. Prescribed JAK inhibitors
3. Contraindication to cessation of bDMARDs (e.g. active, sight-threatening uveitis)
4. Current, active tuberculosis in the immediate or close family or household members
5. Plans to move in the first 6 months after birth with their infant to live in a country with a high rate of tuberculosis (incidence >40 per 100,000 population)

For Infant Inmmunology (optional element):
6. Temporary exclusion criteria for taking immunology samples from the babies - fever in previous 72 hours (or felt to be systemically unwell)

Date of first enrolment
10/02/2025

Date of final enrolment
31/08/2028

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust
Doncaster Royal Infirmary
Armthorpe Road
Doncaster
United Kingdom
DN2 5LT

Study participating centre
Oxford University Hospitals
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Liverpool Women's NHS Foundation Trust
Liverpool Womens Hospital
Crown Street

Liverpool
United Kingdom
L8 7SS

Study participating centre
University Hospitals of Leicester NHS Trust
Leicester Royal Infirmary
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Study participating centre
Manchester University NHS Foundation Trust
Cobbett House
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M13 9WL

Study participating centre
Kettering General Hospital NHS Foundation Trust
Rothwell Road
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NN16 8UZ

Sponsor information

Organisation
University of Oxford

Sponsor details
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Sponsor type
University/education

Website
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ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. Peer reviewed scientific journals
2. Conference presentation
3. Publication on website
4. Submission to regulatory authorities
5. Other
6. Data sharing requests can be made at the end of the research in line with the NPEU Data sharing policy.

Intention to publish date
28/02/2031

Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date