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

Aim

To answer the research question: Is there a difference in arthritis disease control between women who continue their biologic disease-modifying anti-rheumatic drugs (bDMARDs) throughout pregnancy, compared to those who are asked to stop before the third trimester?

The trial aims to recruit 328 women over a 48-month recruitment period in approximately 35 obstetric units with a maternal medicine service in the UK.

Intervention

MAMA 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:

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.

Eligibility

Pregnant women with Autoimmune Inflammatory Arthritis (AIA), satisfying the following criteria:

- Have a diagnosis of rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA)
- Pregnant at less than 28 completed weeks' gestation
- Prescribed a regularly dosed biologic disease-modifying anti-rheumatic drug (bDMARD) for RA, JIA, PsA or axSpA
- Aged 16 years or over
- Has provided informed consent

Primary outcome

Peak disease activity between randomisation and 6 months after the end of pregnancy (measured by the highest RAPID3 total score)

Secondary outcome

- Peak of disease activity up to 12 months after the end of pregnancy
- Other features of arthritis disease activity from randomisation up to 24 months after the end of pregnancy
- Pregnancy outcomes up to hospital discharge after the end of pregnancy
- Neonatal outcomes in babies born to women up to 3 months post-delivery
- Infant and child outcomes including global development at 24 months of age, infection, infant death, and duration of breastfeeding up to 24 months of age, and in a subset of infants to investigate Immune function (including response to vaccines) at 2, 5 and 13 months
- Economic evaluation up to 24 months after the end of pregnancy
- Assessment of acceptability to women and clinicians will be developed using co-applicants and patient and public involvement advisory group)

Number of participants required:	328		
Recruitment start/planned:	September 2024	Recruitment finish/planned:	August 2028
Number of centres:	35		
Funding source:	NIHR Health Technology Assessment (HTA) programme		

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

Inclusion criteria

- Have a diagnosis of rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA)
- Pregnant at less than 28 completed weeks' gestation
- Prescribed a regularly dosed biologic disease-modifying anti-rheumatic drug (bDMARD) (including biologic originators and biosimilars) for RA, JIA, PsA or axSpA
- Aged 16 years or over
- Has provided informed consent

Exclusion criteria

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

Randomisation (1:1 allocation ratio) Secure online randomisation

INTERVENTION
Continuing bDMARDs throughout pregnancy

OR

COMPARATOR
Stopping bDMARDs before the third trimester (28 weeks) of pregnancy, and restarting no earlier than 2 weeks after the end of pregnancy

Primary Outcome

Peak disease activity between randomisation and 6 months after the end of pregnancy (measured by the highest RAPID3 total score)

Secondary outcomes

Peak disease activity from randomisation up to 12 months after the end of pregnancy (measured by the highest RAPID3 total score)

Other features of arthritis disease activity, measured by:

- Peak pain level measured by the highest RAPID3 pain score (from randomisation up to 6 months after the end of pregnancy)
- Peak overall wellbeing measured by the highest RAPID3 patient global estimate score (from randomisation up to 6 months after the end of pregnancy)
- Any occurrence of arthritis flare (from randomisation up to 6 months after the end of pregnancy)
- Need for escalation of therapy due to inflammatory disease activity (from randomisation up to 6 months after the end of pregnancy)
- Any use of NSAIDs and frequency of use for treatment of joint pain (from randomisation up to 6 months after the end of pregnancy)*
- Any occurrence of arthritis flare (from randomisation up to 12 months after the end of pregnancy)*
- Health related quality of life measured using EQ-5D-5L (at 3, 6, 12 and 24 months after the end of pregnancy)
- Anxiety and depression measured using the EQ-5D-5L (at 3, 6, 12 and 24 months after the end of pregnancy)

Pregnancy outcomes (up to hospital discharge after the end of pregnancy)

- Livebirth
- Stillbirth (fetal loss greater than or equal to 24 weeks gestation)
- Pregnancy loss less than 24 weeks gestation*
- Termination of pregnancy (with or without known congenital anomaly)
- Mode of birth*
- Preterm prelabour rupture of membranes*
- New diagnosis of pre-eclampsia*
- New diagnosis of gestational diabetes*
- Venous thromboembolism*
- Confirmed or suspected maternal infection*

Pregnancy outcomes (up to hospital discharge after the end of pregnancy)

- Livebirth
- Stillbirth (fetal loss greater than or equal to 24 weeks gestation)
- Pregnancy loss less than 24 weeks gestation*
- Termination of pregnancy (with or without known congenital anomaly)
- Mode of birth*
- Preterm prelabour rupture of membranes*
- New diagnosis of pre-eclampsia*
- New diagnosis of gestational diabetes*
- Venous thromboembolism*
- Confirmed or suspected maternal infection*

Neonatal outcomes

- Gestational age (continuous) and preterm birth at: <28, 28 to <32 and 32 to 37 gestational weeks 24 months of age
- Birth weight z-score
- Early-onset neonatal infection (up to 72 hours after birth)
- Late-onset infection (>72 hours after birth, up to 28 days postnatal age)
- Received intensive care (up to discharge from neonatal care)*
- Necrotising enterocolitis (up to discharge from neonatal care)*
- Brain injury (up to discharge from neonatal care)*
- Chronic lung disease (up to discharge from neonatal care)*
- Retinopathy of prematurity requiring treatment (up to discharge from neonatal care)*
- Any congenital anomaly (up to 3 months post delivery)*

Infant and child outcomes

- Key long term outcome: child development measured using the Ages and Stages Questionnaire-3 (ASQ-3) 24 month questionnaire total score at 24 months of age
- ASQ-3 score below the cut-off for risk of developmental delay in the 5 domains of development at 24 months of age*
- Number of infections up to 24 months of age
- Duration of breastfeeding up to 24 months of age
- Infant death up to 24 months of age
- Necrotising enterocolitis (up to discharge from neonatal care)*
- Child vaccine/immunological response (for a subset of infants): lymphocyte phenotyping, vaccine-specific antibodies and immunoglobulin levels at 2 months, 5 months and 13 months
- Retinopathy of prematurity requiring treatment (up to discharge from neonatal care)*
- Brain injury (up to discharge from neonatal care)*
- Chronic lung disease (up to discharge from neonatal care)*
- Any congenital anomaly (up to 3 months post delivery)*

Health economic evaluation up to 24 months after the end of pregnancy

- Healthcare utilisation and costs
- Quality-adjusted life years (QALYs)
- Cost-consequence analysis
- Cost-utility analysis
- Child Quality of Life (measured using the PedsQL Total Scale Score)

**(described only using summary statistics)*