

Maralixibat for the treatment of intrahepatic cholestasis of pregnancy

Submission date 16/07/2026	Recruitment status Recruiting	☐ Prospectively registered ☐ Protocol
Registration date 19/10/2026	Overall study status Ongoing	☐ Statistical analysis plan ☐ Results
Last Edited 19/10/2026	Condition category Pregnancy and Childbirth	☐ Individual participant data ☒ Record updated in last year

Plain English summary of protocol

Background and study aims

Intrahepatic cholestasis of pregnancy (ICP) is the most common liver condition that occurs during pregnancy, affecting around 5,500 women each year in the UK. The main symptom is itching, which can range from mild to severe. ICP can increase the risk of complications for the baby, including premature birth (before 37 weeks of pregnancy) and, in the most severe cases, stillbirth.

Researchers have shown these complications are linked to high levels of substances called bile acids, which are produced by the liver to help digest food. In ICP, the normal flow of bile acids from the liver to the gut slows down, causing bile acids to build up in the mother's bloodstream. These bile acids can cross the placenta and reach the baby.

Current treatments for ICP do not work well for everyone. Many women continue to experience significant itching and worry about the health of their baby. Researchers are therefore looking for new treatment options.

Maralixibat is a medicine already used to treat certain liver conditions in children that are associated with itching and high bile acid levels. Studies have shown that it can reduce both itching and bile acid levels. Researchers hope it may have similar benefits for women with ICP. Maralixibat works in the gut by helping the body remove excess bile acids. It is not absorbed into the bloodstream, which means it is not expected to reach other parts of the body. However, because it has not previously been used during pregnancy, it is important to study its safety and effectiveness in pregnant women with ICP.

The METAPHOR study is a Phase 2a/b clinical trial that aims to recruit 28 pregnant women with ICP. The study will investigate:

- How safe maralixibat is during pregnancy
- Whether it reduces itching
- Whether it lowers bile acid levels

Who can participate?

Women may be eligible to take part if they are between 20 weeks and 0 days and 34 weeks and 6 days pregnant.

What does the study involve?

All participants will receive maralixibat, starting with a low dose that can be increased if needed. Throughout the study, researchers will monitor bile acid levels using blood tests and ask participants to complete weekly itch assessments to measure changes in their symptoms. Monitoring will continue until the birth of the baby.

What are the possible benefits and risks of participating?

If maralixibat successfully lowers bile acid levels, it may reduce the risk of serious pregnancy complications in women with very high bile acid levels. It may also improve itching, which can be severe enough to affect sleep and quality of life.

The most common side effect of maralixibat is diarrhoea. To reduce this risk, treatment will begin at a low dose.

Where is the study run from?

Imperial College London (UK).

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

August 2026 to January 2028.

Who is funding the study?

Mirum Pharmaceuticals.

Who is the main contact?

Jenny Chambers / Kelly Brooks

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Additional identifiers

ClinicalTrials.gov (NCT)

NCT07389031

Integrated Research Application System (IRAS)

1012589

Sponsor's protocol code number

180238

Study information

Scientific Title

Maralixibat for the treatment of intrahepatic cholestasis of pregnancy: METAPHOR

Acronym

METAPHOR

Study objectives

Primary objective:

To assess the safety and tolerability of maralixibat for the treatment of intrahepatic cholestasis of pregnancy (ICP) in pregnant women.

We will measure this through the incidence of adverse events (AEs), serious adverse events (SAEs), sudden unexpected serious events,(SUSARs).

Secondary objectives:

To assess the efficacy of maralixibat on pruritus/hypercholanaemia due to ICP on the basis of the following endpoints:

1. Mean change from baseline visit to Visit 3 (21 days on the IMP, minimum 7 days) of the study treatment period in the weekly average worst daily itch score, as measured by the Adult Itch Reported Outcome (5-D Itch Scale)
2. Mean change from baseline visit to Visit 3 (21 days on the IMP) of the study treatment period in total tSBA concentration. Participants who deliver before completing 3 weeks of treatment may be included in the analysis if they receive a minimum of 7 days of treatment
3. Proportion of participants with a composite adverse perinatal outcome
4. Mean change in tSBA concentration and pruritus in participants who continue maralixibat beyond the study outcome endpoint of Visit 3 (21 days on the IMP)
5. Mean change in tSBA concentration and pruritus from the baseline visit of the study treatment period to birth for participants who continue maralixibat beyond Visit 3 (21 days on the IMP)

Ethics approval required

Ethics approval required

Ethics approval(s)

Submitted 15/07/2026, To be confirmed (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; no telephone number provided; -), ref: 26/EM/0167

Primary study design

Interventional

Allocation

N/A: single arm study

Masking

Open (masking not used)

Control

Uncontrolled

Assignment

Single

Purpose

Treatment, Safety

Study type(s)**Health condition(s) or problem(s) studied**

Intrahepatic cholestasis of pregnancy (ICP)

Interventions

All participants will receive maralixibat. Participants will start on a dose of 70mcg/kg/d divided into two doses.

The participants will take the study drug until they give birth so this could be for 1 week up to 21 weeks. They will stop the study med on the day of delivery and return to the hospital for a postnatal check around 4-6 weeks after the birth.

Intervention Type

Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)

Livimarli [Maralixibat (approved INN)]

Primary outcome(s)

Safety and tolerability will be measured by recording the incidence of adverse events (AEs), serious adverse events (SAEs), sudden unexpected serious events,(SUSARs) as they occur (which can be at any timepoint during the study)

Key secondary outcome(s)

Efficacy will be measured at around Visit 3 for participants (around 21 days after starting maralixibat) by assessing the mean change in total serum bile acids (tSBA) and also the mean change in itch which will be recorded weekly using the 5D Itch scale. If participants choose to remain in the study beyond Day 21 the mean change in tSBAs and itch will be assessed from the start of the medication to birth through weekly tSBAs and weekly itch scores (5D Itch scale)

Completion date

27/01/2028

Eligibility

Key inclusion criteria

1. Provide signed informed consent and be willing to comply with all study visits and requirements through to the end of their participation in the study, including the follow-up period if they remain in the trial after Visit 3 (around 21 days on the IMP)
2. Receiving antenatal care at the trust where recruitment and consent are taking place
3. Female aged ≥ 18 years and ≤ 50 years
4. Viable singleton or twin pregnancy between 20 weeks 0 days and 34 weeks 0 days (inclusive) at the screening visit, and no more than 35 weeks 0 days (inclusive) at the baseline visit
5. Diagnosis of ICP, as characterised by the following:
 - 5.1. Onset of pruritus during pregnancy with no known cause other than ICP (e.g., pruritic urticarial papules and plaques of pregnancy, pruritic folliculitis, uncontrolled thyroid disease, etc.)
 - 5.2. Random tSBA concentration ≥ 19 $\mu\text{mol/L}$ within 30 days before the screening visit
 - 5.3. Absence of known pathology that may produce similar laboratory findings/symptoms; these include but are not limited to other cholestatic disorders such as PBC and PSC. Note: women with genetic susceptibility to cholestasis can participate
 - 5.4. Non-fasting (e.g., postprandial) tSBA level ≥ 19 $\mu\text{mol/L}$ as assessed by the local laboratory
6. Willing and able to refrain from the use of any of the following for the duration of the study (following discussion with a clinician from the study team):
 - 6.1. Biologic treatments such as antitumour necrosis factor (TNF) or anti-integrin monoclonal antibodies, or immunosuppressants
 - 6.2. Statins, peroxisome proliferator-activated receptor (PPAR) agonists/fibrate drugs (e.g., fenofibrate, bezafibrate), and S-adenosyl-L-methionine
7. Participants requiring local/systemic corticosteroids or selective serotonin reuptake inhibitors (e.g., sertraline) for the management of non-cholestatic conditions must have been on a stable dose for at least 12 weeks before screening and be willing to remain on a stable dose for the duration of the study to be considered eligible (including steroid use for stable eczema)
8. Administration of isolated doses of corticosteroids for obstetric indications (e.g., promotion of fetal lung maturity for anticipated preterm delivery) is permitted
9. Participants already on a stable dose of UDCA for ICP are considered eligible and can remain on the medication

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Upper age limit

50 Years

Sex

Female

Total final enrolment

0

Key exclusion criteria

1. At the time of either the screening or baseline visit, a decision has been made to deliver within 7 days for any indication
2. Multifetal gestation of triplets or more
3. Known placenta accreta
4. Complete placenta previa
5. Premature rupture of membranes
6. Cervical incompetence
7. History of prior spontaneous birth at ≤ 34 weeks not secondary to known or suspected ICP or another condition (in the opinion of the investigator) likely to result in spontaneous or iatrogenic delivery before 37 weeks
8. Known non-reassuring fetal status based upon antepartum testing (e.g. CTG [cardiotocography]) at or within 7 days before the baseline visit
9. Known fetal anomaly likely to result in intrauterine fetal demise or neonatal death within the first 30 days of life
10. History or evidence (not ICP) of current underlying cholestatic liver disease at screening or baseline, including but not limited to:
 - 10.1. Primary or secondary sclerosing cholangitis
 - 10.2. Primary biliary cholangitis
 - 10.3. Immunoglobulin G4-related cholangitis
 - 10.4. Ascending cholangitis
 - 10.5. Clinical evidence or suspicion of dominant strictures considered clinically relevant by the investigator, or current or planned placement of a percutaneous drain or biliary stent
11. Evidence of other hepatobiliary conditions, including but not limited to:
 - 11.1. Active hepatitis B infection as defined by the presence of hepatitis B surface antigen (HBsAg) or hepatitis B virus DNA
 - 11.2. History or evidence of autoimmune hepatitis, Wilson disease, alpha-1-antitrypsin deficiency, haemochromatosis, or drug-induced liver disease (as defined on the basis of typical exposure and history)
 - 11.3. Evidence or clinical suspicion of cirrhosis, including compensated or decompensated cirrhosis (e.g. hepatic encephalopathy, portal hypertension, hepatorenal syndrome, hepatopulmonary syndrome, oesophageal varices, ascites)
 - 11.4. Suspected or proven cholangiocarcinoma or hepatocellular carcinoma
 - 11.5. History of liver transplantation
 - 11.6. Acute fatty liver of pregnancy
 - 11.7. Severe pre-eclampsia or HELLP syndrome (EHTN and PIH are not exclusion criteria)
 - 11.8. Alcohol-related liver disease
12. History or presence of known or suspected inflammatory bowel disease (e.g. Crohn's disease or ulcerative colitis). IBS is not an exclusion criterion
13. History of small bowel resection, bariatric surgery (e.g. gastric bypass or gastric banding), or

other surgery resulting in disruption of the enterohepatic circulation

14. Presence of any concurrent underlying condition with unstable pruritus, including but not limited to unstable atopic dermatitis, psoriasis, urticaria, psychogenic pruritus, or active severe eczema. Participants with stable pruritic conditions that pre-date pregnancy and who have been on stable doses of treatment for at least 12 weeks before screening may be considered eligible

15. Anticipated need for liver transplantation within 12 months after enrolment

16. Active infection that, in the opinion of the investigator, precludes participation in the study for participant safety reasons

17. Unstable and/or serious medical disease likely to impair the participant's ability to participate in all aspects of the study or result in substantially shortened life expectancy (e.g. malignancy or end-stage heart failure)

18. Known diagnosis of HIV infection, or HIV antibody positivity

19. Clinically relevant alcohol use disorder or substance abuse within 12 months before screening

20. General anaesthesia within 3 months before screening (to exclude the unlikely possibility of halothane exposure)

21. Participant has any of the following laboratory parameters during the current pregnancy:

21.1. Platelet count $\leq 100,000/\text{mm}^3$

21.2. Serum creatinine $\geq 77 \mu\text{mol/L}$ (0.87 mg/dL)

21.3. ALT or AST $> 300 \text{ IU/L}$

21.4. Total bilirubin $> 50 \mu\text{mol/L}$, unless the participant is known to have Gilbert's syndrome or haemolytic anaemia

21.5. INR ≥ 1.3 , unless due to therapeutic anticoagulation

22. Except as defined elsewhere in the inclusion or exclusion criteria, abnormal laboratory results are exclusionary only if they are deemed clinically significant and to place the participant at unacceptable risk from study participation, as determined by the investigator

23. Use within 12 weeks (or within 5 half-lives, whichever is greater) of any of the following medications:

23.1. Methotrexate

23.2. Sodium phenylbutyrate

23.3. PPAR agonists (e.g. fibrates)

23.4. Known hepatotoxins (e.g. ciclosporin, tacrolimus, JAK inhibitors, pancreatic lipase inhibitors when dosed systemically)

24. Use within 1 week (or within 5 half-lives, whichever is greater) of the following medications when dosed systemically:

24.1. Progesterone supplementation

24.2. Cholestasis-inducing medications, including but not limited to erythromycin, amoxicillin-clavulanate, ACE inhibitors, or terbinafine

25. Breastfeeding at the time of enrolment or planning to breastfeed during the study

26. Known intolerance or hypersensitivity to maralixibat and/or its excipients:

26.1. Propylene glycol (E1520)

26.2. Disodium edetate

26.3. Sucralose

26.4. Grape flavour

26.5. Purified water

27. Confirmed positive urine drug or alcohol screen at any time during pregnancy

28. History of non-adherence

Date of first enrolment

23/08/2026

Date of final enrolment

17/12/2027

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

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England

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Sponsor information

Organisation

Imperial College London

ROR

<https://ror.org/041kmwe10>

Funder(s)

Funder type

Funder Name

Mirum Pharmaceuticals

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be available upon reasonable request from the Chief Investigator and Imperial College London (Sponsor). De-identified individual participant data underlying the published results, together with supporting study documents where appropriate (e.g. the study protocol and statistical analysis plan), will be made available following publication of the primary study results. Requests will be considered for scientifically sound research, subject to Sponsor approval, appropriate data sharing

agreements, participant consent, and applicable ethical, legal, and regulatory requirements. Data will be shared in an anonymised form to protect participant confidentiality.

IPD sharing plan summary

Available on request