ISRCTN13610566 https://doi.org/10.1186/ISRCTN13610566

A study to test if LACTIN-V, a type of probiotic made from a specific bacteria (Lactobacillus crispatus CTV-05), is safe and effective in lowering the chances of preterm labour in women who are considered at high risk for giving birth early

Submission date 20/09/2025	**Recruitment status** Not yet recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 08/12/2025	**Overall study status** Ongoing	
Last Edited 23/01/2026	**Condition category** Pregnancy and Childbirth	

Plain English summary of protocol

Background and study aims

Spontaneous preterm birth occurs when a mother goes into labour before 37 weeks. Early preterm birth (babies born before 34 weeks) is an important cause of the death of newborn babies, and long-term disability in some of those who survive. There is now good evidence that the type of bacteria in the mother's vagina during pregnancy can affect the risk of preterm birth. The presence of lactobacilli (except for one particular type; lactobacillus iners) helps protect against early birth. The type lactobacillus crispatus, in particular, is linked to the lowest risk of preterm birth. On the other hand, having lactobacillus iners or no lactobacilli at all increases the risk of preterm birth.

We have found that vaginal administration of a strain of lactobacillus crispatus (called CTV-05) using during pregnancy leads to growth of this bacteria in the vagina, and in most cases replacing lactobacillus iners or other bacteria present in the vagina. The new lactobacillus crispatus will remain present for the whole of the pregnancy. In this study, we will determine whether administration of lactobacillus crispatus CTV-05 will reduce the risk of preterm birth.

Who can participate?

Women who have been predefined as at high risk because they had a previous preterm birth or previous second trimester loss, seen in preterm birth prevention clinics in NHS hospitals.

What does the study involve?

Participants will be randomly allocated to be given either vaginal CTV-05 or an identical inactive substance (placebo) during their pregnancy. The main outcome will be to determine the rates of preterm birth in the two groups. However, the researchers will also take vaginal swab samples and blood tests to look at the effect of CTV-05 or placebo on the bacteria present within the

vagina and how that links to the risk of preterm birth. The study will take up to 3 years to recruit all of the participants from four hospitals in London and for all of their pregnancy outcomes to become known.

What are the possible benefits and risks of participating?
It is proposed that use of LACTIN-V will reduce the risk of preterm birth, although as this is not yet proven, there is no known benefit to you taking part in this trial. We cannot say that taking part in this trial will help you directly. Other pregnant women may benefit from the results of this research in the future.
Associated risks from participation in this trial center mainly around the possibility of known and unknown side effects of the IMP. We have demonstrated that LACTIN-V has high tolerability, and safety in a cohort of pregnant women at high-risk of PTB (as part of the FLIP-1 study). To date, there has been a considerable amount of experience using LACTIN-V at concentrations up to 2 x 109 CFU/dose without any apparent related adverse effects, with the exception of a short duration of vaginal discharge. Risks from the administration of LACTIN-V are considered to be low, given that colonisation with this type of organism is strongly associated with improved vaginal health. No systemic risks are anticipated since this is an organism that is applied topically, and not absorbed systemically. These risks will be explained in the written informed sheet. Any allergic-type reactions to the study product, including anaphylaxis, will be managed in accordance with current standard clinical practice. If these events occur the participant will immediately discontinue the study, and the event will be recorded in an adverse event form. Participants with known allergy to any of the components of the study product will be excluded from enrolment.
Participants may experience discomfort during examination when required for vaginal swab collection. The transvaginal ultrasound would be completed as standard of care regardless of participation in the trial. Participants may also experience discomfort during or following the undertaking of phlebotomy for blood samples during this study, which may be associated with feeling faint or dizzy, and associated local traumatic impacts from venipuncture sites such as bruising, swelling and rarely, infection.
Owing to the ‘high-risk’ of PTB status of participants, they may experience worry or anxiety in relation to results of transcervical length scanning, whereby the results of these scans may indicate an increasing risk of PTB.
There are no additional visits beside those completed as part of routine antenatal care and follow-up post birth. The final study visit prior to birth at 36+0 - 38+6 weeks, may be completed remotely over the phone where the treating team deem this appropriate. This will reduce the burden on participants when they are heavily pregnant. All additional study procedures are completed at routine ultrasound appointments or post-natal appointments.
Transvaginal ultrasound, transabdominal ultrasound and sample collection will be undertaken only by appropriately trained and experienced staff to minimise discomfort.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
September 2025 to December 2027

Who is funding the study?
1. March of Dimes Foundation
2. NIHR BRC (UK)

Who is the main contact?
1. Dr Lynne Sykes, l.sykes@imperial.ac.uk
2. Imperial Clinical Trials Unit, flip2@imperial.ac.uk

Contact information

Type(s)
Scientific, Principal investigator

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Public

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Additional identifiers

Integrated Research Application System (IRAS)
1010339

Central Portfolio Management System (CPMS)
65138

Protocol serial number
175343

Study information

Scientific Title
FLIP-2: A placebo-controlled double blinded randomised trial to assess the safety and efficacy of LACTIN-V, a live biotherapeutic Lactobacillus crispatus strain CTV-05, in reducing the risk of preterm labour in a cohort of women predefined as at high risk

Acronym
FLIP-2

Study objectives
Primary objective:
To determine whether vaginal administration of live biotherapeutic L.crispatus CTV-05 (LACTIN-V) in the second trimester of pregnancy in women at high risk of preterm birth leads to a reduced incidence of preterm birth <37 weeks gestation.

Secondary objectives:
1. To determine whether LACTIN-V is associated with a reduction in the risk of cervical shortening (< or equal to 25 mm in the second trimester (16+0 to 28+0 weeks gestation).
2. To determine whether LACTIN-V is associated with a reduced incidence of preterm birth pregnancy loss 16+0 to 34+0 weeks gestation.
3. To identify whether LACTIN-V in the second trimester is associated with a reduced incidence of PPROM < 34 and <37 weeks of pregnancy.
4. To compare average gestational age at delivery between arms.
5. To compare the incidence of a neonatal outcome consisting of a composite of death, brain injury, or bronchopulmonary dysplasia (neonatal) between arms.
6. To compare the incidence of early onset neonatal sepsis between arms.
7. To assess developmental progress of the child at 2 years of age (using the Parent Report of Children's Abilities (PARCA-R) parent questionnaire).
8. To compare the safety profile/outcomes between arms.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 05/12/2025, London - Harrow Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; -; Harrow.rec@hra.nhs.uk), ref: 25/LO/0766

Study design
Double-blind randomized placebo-controlled trial

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Preterm labour

Interventions

LACTIN-V is supplied as a pre-filled, single-use vaginal applicator. Each applicator contains 200 mg of LACTIN-V powder at a dose of 2 x 109 CFU. The LACTIN-V powder formulation contains L. crispatus CTV-05, trehalose, xylitol, sodium ascorbate, colloidal silicon dioxide, and maltodextrin.

The placebo for this trial will consist of an identical appearing inert powder delivered via the same single-use applicator.

The study drug will be administered as an initial loading phase followed by a maintenance phase. The first five doses will occur on five consecutive days, which is referred to the 'loading phase'. Further single doses will be given at once-weekly intervals (calculated 1 week from the 5th consecutive dose) up to the 34th week of pregnancy. This is referred to as the 'maintenance phase'.

Participants are randomised using Sealed Enveloped incorporated into the OpenClinica eCRF system. All participants are followed up until the birth of their baby. At 24 months of age, parents will be invited to complete the online PARCA-R questionnaire, which serves as a tool of assessing developmental outcomes in children.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
LACTIN-V (Lactobacillus crispatus CTV-05)

Primary outcome(s)
The rate of preterm birth, defined as delivery occurring before 37 completed weeks of pregnancy, measured at end of study and any interim reports to the data monitoring committee (DMC)

Key secondary outcome(s))
1. Incidence of cervical shortening (< or equal to 25 mm), measuring using transvaginal ultrasounds at the end of the study and any interim reports to the data monitoring committee (DMC)
2. The rate of preterm birth, defined as delivery occurring before 34 completed weeks of pregnancy measured at the end of study and any interim reports to the data monitoring committee (DMC)
3. Incidence of preterm prelabour rupture of membranes (PPROM) <34 weeks, measured at the end of study and any interim reports to the data monitoring committee (DMC)
4. Mean and median gestational age at delivery, measured at the end of study and any interim reports to the data monitoring committee (DMC)
5. Incidence of a neonatal outcome consisting of a composite of death, brain injury, or bronchopulmonary dysplasia (neonatal), measured at the end of study and any interim reports to the data monitoring committee (DMC)
6. Incidence of early onset neonatal sepsis measured through reported adverse events, measured at the end of study and any interim reports to the data monitoring committee (DMC)
7. Developmental progress of the child, measured using the Parent Report of Children's Abilities

(PARCA-R) parent questionnaire at 2 years of age
8. Safety assessment, measured through reported adverse events at end of study and any interim reports to the data monitoring committee (DMC)

Measured at end of study and any interim reports to the data monitoring committee (DMC) or 2 years from birth of the child

Completion date
31/12/2027

Eligibility

Key inclusion criteria
1. Women confirmed to be at risk of preterm labour, as defined by previous preterm birth and/or mid trimester loss
2. Able to provide written, informed consent
3. Confirmed viable intrauterine singleton pregnancy between 12-16 weeks gestational age

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Total final enrolment
0

Key exclusion criteria
1. Women living with HIV
2. Women under the age of 17 years (updated 23/01/2026, previously under the age of 18 years)
3. Women with a multiple pregnancy
4. Known allergy or sensitivity to the investigational product
5. Participants taking part in an alternative interventional research study
6. Known congenital/structural or chromosomal anomaly
7. Women with deep epithelial disruption observed on genital examination on or before the day of randomisation
8. Women with any condition requiring regular periodic use of systemic antibiotics during participation in the trial
9. Women with any social, medical, or psychiatric condition that in the opinion of the Investigator would complicate the evaluation or make it unlikely for the subject to comply with the study protocol
10. Use of immunosuppressive drugs within 60 days of randomisation

Date of first enrolment

09/02/2026

Date of final enrolment
30/04/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St Mary's Hospital
Praed Street
London
England
W2 1NY

Study participating centre
Queen Charlotte's Hospital
Du Cane Road
London
England
W12 0HS

Study participating centre
Uclh
250 Euston Road
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NW1 2PQ

Study participating centre
Chelsea and Westminster Hospital
369 Fulham Road
London
England
SW10 9NH

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Charity

Funder Name
March of Dimes Foundation

Alternative Name(s)
March of Dimes, MDF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes