

# 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

<b>Submission date</b> 20/09/2025	<b>Recruitment status</b> Not yet recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 08/12/2025	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 08/12/2025	<b>Condition category</b> Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## 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  $2 \times 10^9$  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

### Contact name

Dr Lynne Sykes

### Contact details

Du Cane Road  
London  
United Kingdom  
W12 0HS  
+44 (0)20 7594 2141  
l.sykes@imperial.ac.uk

### Type(s)

Public

### Contact name

Imperial Clinical Trials Unit

### Contact details

Imperial College London  
1st Floor Stadium House (Entrance A)  
68 Wood Lane  
London  
United Kingdom  
W12 7RH  
-  
flip2@imperial.ac.uk

## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### Integrated Research Application System (IRAS)

1010339

### ClinicalTrials.gov (NCT)

Nil known

### 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)

notYetSubmitted

## 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  $2 \times 10^9$  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 Envelopes 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 ( $\leq$  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 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**

05/01/2026

**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

London

England

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?
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes