

# The New Horizons Study

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| <b>Submission date</b><br>20/09/2022   | <b>Recruitment status</b><br>No longer recruiting     | <input checked="" type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol            |
| <b>Registration date</b><br>28/10/2022 | <b>Overall study status</b><br>Ongoing                | <input type="checkbox"/> Statistical analysis plan<br><input type="checkbox"/> Results                       |
| <b>Last Edited</b><br>09/01/2025       | <b>Condition category</b><br>Pregnancy and Childbirth | <input type="checkbox"/> Individual participant data<br><input type="checkbox"/> Record updated in last year |

## Plain English summary of protocol

### Background and study aims

Women are at increased risk of blood clots, in the veins of the legs and the blood vessels of the lungs, after having a baby for up to 6 weeks. Women who are identified at high risk of developing these blood clots are given anticoagulant treatment at a low dose to try and prevent them. Currently, the only treatments we know to be safe in breastfeeding women is an injectable medication (low molecular weight heparin) or a tablet which needs frequent blood testing (warfarin). Both options have pros and cons associated with them, making life difficult for women. In recent years new anticoagulant tablets have become available, called direct oral anticoagulants (DOACs) however little information exists on how much of these new medications distribute into breastmilk. This research study builds on our previous work and will:

- look at how 2 of these new medicines (rivaroxaban and edoxaban) gets into breastmilk of women who have recently had their child, and
- assess whether it would be safe for women to breastfeed safely, when on these medications.

### Who can participate?

Women aged 18 years and older who have given birth in the previous 12 weeks.

### What does the study involve?

Volunteers will be assigned either rivaroxaban 20 mg DAILY or edoxaban 60 mg DAILY. They will be asked to take the medicine for 3 consecutive days and have their blood and breastmilk sampled.

### What are the possible benefits and risks of participating?

#### Benefits:

Participation will help women in the future who require blood thinning medication after delivering their baby.

#### Risks:

The key risks associated with this study are:

- (i) giving volunteers doses of anticoagulants for 3 days when it is not indicated.
- (ii) asking the women to stop breastfeeding, whilst they take part in the study.
- (iii) multiple blood samples over a 72 hour period.
- (iv) no information on edoxaban's transfer into human breastmilk exists.

Addressing (i) - both rivaroxaban and edoxaban are widely prescribed around the world for the prevention and treatment of blood clots. Their side-effect profiles are well described and

although the women in question have no indication for the anticoagulant, the absolute risk to them of taking the medication is extremely low. Our research team will be very clear when outlining the study to women, what the risks are to them and give them ample time to discuss with their family and friends, before they make their decision.

Regarding (ii) - as there is a lack of robust information on how rivaroxaban and edoxaban distributes into breastmilk, we have no choice but to ask women to cease breastfeeding for the time they are taking these agents. This aspect of the study will be made clear to women. Our experience from the previous work was, that women did re-commence breastfeeding, once we had given them the all clear. When at all possible, we will encourage women to express milk before the study, so they can use when the sampling is taking place.

For (iii) - we have kept the sampling times, as minimal as possible whilst ensuring that all the requisite information is obtained in order to answer the research questions posed. Like in our previous work, we will do home sampling for women, so the burden of travelling to the hospital is removed for them.

(iv) - volunteers assigned edoxaban, after 2 have been sampled, we will conduct an interim analysis to see how much transfers into milk. If it appears that significant transfer occurs, this arm of the trial will cease. A 'go-no go' element in the design of the study has been built in.

Where is the study run from?

King's College Hospital Foundation NHS Trust (UK)

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

July 2022 to December 2026

Who is funding the study?

King's College Hospital Foundation NHS Trust (UK)

Who is the main contact?

Prof. Roopen Arya, roopen.arya@nhs.net

## Contact information

### Type(s)

Scientific

### Contact name

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### Type(s)

Principal investigator

**Contact name**

Prof Roopen Arya

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## **Additional identifiers**

**Clinical Trials Information System (CTIS)**

Nil known

**Integrated Research Application System (IRAS)**

1005067

**ClinicalTrials.gov (NCT)**

Nil known

**Protocol serial number**

3631, IRAS 1005067

## **Study information**

**Scientific Title**

Can edoxaban and rivaroxaban be prescribed for breastfeeding mothers?

**Study objectives**

Current study hypothesis as of 20/02/2024:

Primary objective:

To determine if edoxaban and rivaroxaban are excreted in breastmilk to clinical relevant concentrations when breastfeeding women take the IMP for 3 consecutive days within the 12-week postpartum period.

Secondary objectives:

1. To describe the concentration-time profiles of edoxaban and rivaroxaban in the plasma and breastmilk of breastfeeding mothers within the 8-week postpartum period, following daily dosing for 3 consecutive days and therefore to establish the potential exposure of breastfed infants to edoxaban and rivaroxaban.
2. To determine the extent of edoxaban transfer into human breastmilk within the 12-week postpartum period.
3. To determine the extent of rivaroxaban transfer into human breastmilk within the 12-week postpartum period.

Previous study hypothesis:

Primary objective:

To determine if edoxaban and rivaroxaban are excreted in breastmilk to clinical relevant concentrations when breastfeeding women take the IMP for 3 consecutive days within the 8-week postpartum period.

Secondary objectives:

1. To describe the concentration-time profiles of edoxaban and rivaroxaban in the plasma and breastmilk of breastfeeding mothers within the 8-week postpartum period, following daily dosing for 3 consecutive days and therefore to establish the potential exposure of breastfed infants to edoxaban and rivaroxaban.
2. To determine the extent of edoxaban transfer into human breastmilk within the 8-week postpartum period.
3. To determine the extent of rivaroxaban transfer into human breastmilk within the 8-week postpartum period.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Approved 07/10/2022, North West - Liverpool Central Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 2071048016; liverpoolcentral.rec@hra.nhs.uk), ref: 22/NW/0273

### **Study design**

Single-centre open-label non-randomized

### **Primary study design**

Observational

### **Study type(s)**

Treatment

### **Health condition(s) or problem(s) studied**

Treatment and prevention of blood clots following the birth of a baby

### **Interventions**

Volunteers will be assigned either rivaroxaban 20mg DAILY or edoxaban 60mg DAILY. They will be asked to take the medicine for 3 consecutive days and have their blood and breastmilk sampled. The sampling times are as follows:

Day 1 (hr): 3, 12, 24

Day 3 (hr): 0, 3, 12, 24, 72

### **Intervention Type**

Drug

### **Phase**

Phase IV

### **Drug/device/biological/vaccine name(s)**

Edoxaban, rivaroxaban

**Primary outcome(s)**

Edoxaban and rivaroxaban concentrations in plasma and breastmilk at the sampled time-points.

Day 1: Time (hr) 3, 12, 24

Day 3: Time (hr) 0, 3, 12, 24, 72

**Key secondary outcome(s)**

The following PK parameters for edoxaban and rivaroxaban in milk and plasma will be computed: Area under the concentration-time curve (AUC) from zero to 24 hours (AUC(0-24)) on day 1 and day 3 for both breastmilk and maternal plasma.

In addition Milk:Plasma ratio will be computed at day 1 and day 3.

**Completion date**

31/12/2026

**Eligibility****Key inclusion criteria**

Current inclusion criteria as of 20/02/2024:

1. Subject is informed and given ample time and opportunity to think about her participation and has provided written informed consent for participation in the study before any study-specific procedures take place.
2. Subject is considered reliable and capable of adhering to applicable protocol requirements, including the study drug being administered orally and visit schedule according to the judgement of the Investigator.
3. Women are aged  $\geq 18$  years.
4. Within the 12-week postpartum period, with the final dose of the IMP being administered and sampled within 12 weeks post-partum.
5. Decision has been confirmed by the participant to hold breastfeeding their infant during the study period.
6. Negative pregnancy test.
7. Good physical and mental health, in the opinion of the Investigator, determined on the basis of medical history and general clinical examination at Screening.
8. Women have clinical laboratory test results within the reference ranges of the testing laboratory: normal renal and liver function, as judged by the chief investigator.
9. Women are not taking any medication interacting with edoxaban or rivaroxaban.
10. Women are available and permit the research team to make home visits to collect blood and milk samples.
11. Women agree to the study restrictions.

**Previous inclusion criteria:**

1. Subject is informed and given ample time and opportunity to think about her participation and has provided written informed consent for participation in the study before any study-specific procedures take place.
2. Subject is considered reliable and capable of adhering to applicable protocol requirements, including the study drug being administered orally and visit schedule according to the judgement of the Investigator.
3. Women are aged  $\geq 18$  years.
4. Within the 8-week postpartum period, with the final dose of the IMP being administered and sampled within 8 weeks post-partum.
5. Decision has been confirmed by the participant to hold breastfeeding their infant during the

study period.

6. Negative pregnancy test.

7. Good physical and mental health, in the opinion of the Investigator, determined on the basis of medical history and general clinical examination at Screening.

8. Women have clinical laboratory test results within the reference ranges of the testing laboratory: normal renal and liver function, as judged by the chief investigator.

9. Women are not taking any medication interacting with edoxaban or rivaroxaban.

10. Women are available and permit the research team to make home visits to collect blood and milk samples.

11. Women agree to the study restrictions.

### **Participant type(s)**

Healthy volunteer

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Sex**

Female

### **Key exclusion criteria**

1. Women who are unable to provide written informed consent.

2. LMWH thromboprophylaxis is indicated.

3. Increased risk of bleeding for any reason.

4. Known contra-indications to edoxaban or rivaroxaban.

5. On-going treatment with aspirin, NSAIDs or other drugs that affect blood clotting.

6. Treatment with significant P-GP / CYP3A4 inducers or inhibitors.

7. Patients who have received an artificial heart valve, have had a heart attack or suffer an irregular heartbeat.

8. Known impaired renal function.

9. Known abnormal liver function tests.

10. Known hypersensitivity or allergy to edoxaban or rivaroxaban.

11. Use of other investigational study drugs within 7 days prior to study entry.

### **Date of first enrolment**

01/04/2023

### **Date of final enrolment**

31/12/2025

## **Locations**

### **Countries of recruitment**

United Kingdom

England

**Study participating centre**

**King's College Hospital**

King's College Hospital NHS Foundation Trust

Denmark Hill

London

United Kingdom

SE5 9RS

## Sponsor information

**Organisation**

King's Health Partners Clinical Trials Office

## Funder(s)

**Funder type**

Hospital/treatment centre

**Funder Name**

King's College Hospital NHS Foundation Trust

**Alternative Name(s)**

**Funding Body Type**

Government organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

United Kingdom

## Results and Publications

**Individual participant data (IPD) sharing plan**

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

**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="#">HRA research summary</a>          |                               |              | 28/06/2023 | No             | No              |
| <a href="#">Participant information sheet</a> | Participant information sheet | 11/11/2025   | 11/11/2025 | No             | Yes             |