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The New Horizons Study

Submission date
20/09/2022

Recruitment status
Recruiting

Registration date
28/10/2022

Overall study status
Ongoing

Last Edited
09/01/2025

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] 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

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Type(s)

Principal Investigator

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Prof Roopen Arya

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1005067

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
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

Secondary study design
Pharmacokinetic

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

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

Pharmaceutical study type(s)
Pharmacokinetic

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Edoxaban, rivaroxaban

Primary outcome measure
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

Secondary outcome measures
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.

Overall study start date
28/07/2022

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 ≥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 ≥18 years.
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11. Women agree to the study restrictions.

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
12

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
England

United Kingdom

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

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Sponsor type

University/education

Website
https://www.kch.nhs.uk/

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

Publication and dissemination plan
Peer reviewed scientific journals
Conference presentation
Due to the nature of the study, data will not be shared and consent will not be sought to do so.

Intention to publish date
31/12/2026

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?
HRA research summary			28/06/2023	No	No