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Preterm milk Fortification in Neonates

Submission date 23/04/2021	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 01/10/2021	**Overall study status** Completed	
Last Edited 20/02/2024	**Condition category** Neonatal Diseases	

Plain English summary of protocol

Background and study aims
Preterm and small babies often struggle to grow on breast milk (maternal or donor) alone, and commercially available cows milk-based fortifiers are currently added to breast milk to help growth. A human-based powdered fortifier is now commercially available.

Who can participate?
Infants born at less than 32 weeks gestation who have never received a cows milk-based diet (formula or fortifier) and have established full milk feeds

What does the study involve?
Participants will be allocated to one of two groups, with an equal chance of being in either group (like tossing a coin). Infants in each group will receive one of two nutritionally equivalent fortifiers as a supplement to breast milk for babies born before 32 weeks gestation or weighing less than 1500 g at birth. One fortified supplement will be a standard cows milk-based product and the other a human-based product.

Infants will receive the fortified supplement from the start of the infants being fully fed on breast milk (when they have no intravenous feeds and are tolerating 150 ml/kg/day of milk) until 36 weeks gestation, or when a fortifier is no longer required, whichever is earlier. Mothers in both groups will be fully supported to provide their own breast milk, and any shortfall will be made up with standard human donor milk. No other changes to infant or mother care will take place. This study will compare gut inflammation through measures of stool samples (and blood /urine where available) and other outcomes until discharge from the neonatal unit.

What are the possible benefits and risks of participating?
The study group is preterm infants where growth and gut health are challenging. The study aims to promote optimal growth and minimise gut problems by comparing human milk based fortification to cows milk based fortification. The measures of growth are weight and the measures of gut problems are laboratory measures undertaken on stool. Preterm infants are fortified with cows milk based products currently, the human product is the new intervention and the hope is that because it does not contain non-human protein it will be better tolerated by the infants.

Where is the study run from?
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK) and will be run in neonatal units in 3 UK hospitals

When is the study starting and how long is it expected to run for?
From January 2021 to April 2023

Who is funding the study?
NeoKare Nutrition Ltd (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
293189

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 293189, CPMS 50596

Study information

Scientific Title
Breastmilk fortification in preterm infants: a randomised controlled trial of two nutritionally equivalent fortifiers

Acronym
PUFFIN

Study objectives
Human milk based fortifier for preterm infants will result in less gut inflammation than the standard cow milk based fortifier currently in use in the UK as measured by stool calprotectin

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 21/10/2021, Yorkshire & The Humber - Sheffield Research Ethics Committee (NHS Blood and Transplant Blood Donor Centre, Holland Drive, Newcastle upon Tyne, Tyne and Wear, NE2 4NQ, UK; +44 (0)207 104 8388; sheffield.rec@hra.nhs.uk), ref: 21/YH/0224

Study design
Multi centre non-blinded randomized controlled study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

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

Health condition(s) or problem(s) studied
Preterm gut inflammation and other outcomes of prematurity (growth, length of hospital stay)

Interventions
Babies born at <32 weeks gestation or <1500 g birthweight will be randomised using Sealed envelope (a commercial randomisation company) to one of two groups to receive:
1. Standard cows milk-based fortified supplement to breast milk
2. Human-based product fortified supplement to breast milk

The intervention will run from when the infants are being fully fed on breast milk (when they have no intravenous feeds and are tolerating 150 ml/kg/day of milk) until 36 weeks gestation, or when a fortifier is no longer required, whichever is earlier. Mothers in both groups will be fully

supported to provide their own breast milk, and any shortfall will be made up with standard human donor milk. No other changes to infant or mother care will take place. This study will compare gut inflammation through measures of stool samples (and blood/urine where available) and other outcomes until discharge from the neonatal unit.

Intervention Type
Supplement

Primary outcome measure
Faecal calprotectin measured from stool samples collected at baseline and 1 and 3 weeks after the intervention (until 36 weeks gestation, or when a fortifier is no longer required, whichever is earlier)

Secondary outcome measures
1. Faecal sIgA, cytokine panel, and bacterial taxa (by 16srRNA) measured from stool samples collected at baseline and 1 and 3 weeks after intervention
2. Infant health measured using records of growth, morbidities associated with preterm birth, length of hospital stay, and biochemical results between baseline until discharge from the neonatal unit

Overall study start date
01/01/2021

Completion date
28/04/2023

Eligibility

Key inclusion criteria
1. Born at <32 weeks gestation
2. Never received cow milk-based diet (formula or fortifier) and having established full milk feeds

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
36

Key exclusion criteria
1. Previous necrotising enterocolitis or gut surgery or malformation
2. Previous receipt of cow milk based diet (formula or fortifier)

Date of first enrolment
01/03/2022

Date of final enrolment
28/02/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Newcastle upon Tyne Hospitals NHS Foundation Trust
Neonatal Unit (Ward 35)
Royal Victoria Infirmary
Richardson Road
Newcastle
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NE1 4LP

Study participating centre
James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
University Hospital Southampton NHS Foundation Trust
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Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

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Richardson Road
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Sponsor type
Hospital/treatment centre

Website
http://www.newcastle-hospitals.org.uk/

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Industry

Funder Name
NeoKare Nutrition Ltd

Results and Publications

Publication and dissemination plan
We aim to publish in peer reviewed journals. Participants will be signposted to results via websites but not individually informed.

Intention to publish date
28/04/2024

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date