

Paediatric Accelerator Mass Spectrometry evaluation research study (midazolam)

Submission date 04/06/2014	Recruitment status No longer recruiting	☐ Prospectively registered ☐ Protocol
Registration date 23/06/2014	Overall study status Completed	☐ Statistical analysis plan ☐ Results
Last Edited 13/03/2017	Condition category Other	☐ Individual participant data ☐ Record updated in last year

Plain English summary of protocol

Background and study aims

This is done using a technique called microdosing, where the dose of the drug given is too small to cause whole-body effects, but large enough to allow researchers to see what happens to the drug inside the body. This includes how the body affects the drug, how the drug is absorbed and distributed, whether any chemical changes to the drug occurs and, finally, how the drug is removed, or excreted, from the body. All this is achieved with little risk of bad side effects, due to the dose being so low. Here, a method called microtracer dosing, where the drug midazolam is labelled with a tiny amount of radiation which is then measured by accelerator mass spectrometry (a technique that shows where the drug is inside the body, and what is happening to it) is used to find out the effects of this drug on newborn, infants and toddlers. The results of this analysis are then compared with information about this drug found through previous research using standard methods. This study could establish a way for accelerator mass spectrometry (AMS) studies to be used for developing new drugs for children, which will mean that such drugs can be given earlier than they are now.

Who can participate?

Babies and toddlers of either sex, between preterm up to 2 years, that have been admitted to hospital.

What does the study involve?

A single microdose of radioactive midazolam will be given either by mouth or injection through a vein. Blood will periodically be taken for testing of the drug and what happens to it once inside the body, over the next twelve hours. The maximum length of participation in the study is up to 48 hours after giving the study drug.

What are the possible benefits and risks of participating?

The participants will not gain any direct benefit. The benefits from this study are for other babies in the future as the information gathered in this study becomes available. The risks due to midazolam will be very small as this dose is less than a millionth of the dose normally given to newborn babies and infants. There are no anticipated safety issues relating to exposure to the radioactive drug.

Where is the study run from?

The study is run from the following sites:

1. Liverpool Women's NHS Foundation Trust (UK) (lead centre)
2. Alder Hey Children's NHS Foundation Trust (UK)

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

June 2014 to December 2014

Who is funding the study?

ERA-NET PrioMedChild (Priority Medicines for Children) (Netherlands)

Who is the main contact?

Dr Mark Turner

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Contact information

Type(s)

Scientific

Contact name

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Contact details

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Additional identifiers

Protocol serial number

LWH0984

Study information

Scientific Title

A multi-centre clinical study to evaluate the use of a microtrace dose of ^{14}C -labelled midazolam and accelerator mass spectrometry (AMS) bioanalysis as new tools in drug development to determine pharmacokinetics in neonates, infants and toddlers

Acronym

PAMS Midazolam

Study objectives

^{14}C -labelled microdose midazolam has similar PK to "cold", standard, therapeutic midazolam

Ethics approval required

Old ethics approval format

Ethics approval(s)

North West REC Liverpool East, 15/04/2014, ref. 13/NW/0839

Primary study design

Observational

Study design

Multicentre observational open-label study

Study type(s)

Other

Health condition(s) or problem(s) studied

Medicines for Children; Paediatrics

Interventions

1. A single ¹⁴C labelled microdose of midazolam will be administered IV or orally. The microdose will contain 111 Bq / kg ¹⁴C labelled midazolam. The ¹⁴C labelled microdose of midazolam will be presented as a sterile solution suitable for oral or intravenous administration.

2. Blood results taken for haematology, biochemistry and blood gas analysis that are required for clinical care. No haematology, biochemistry or blood gas studies samples will be taken for the purposes of this study. The most recent samples will be included in the data if they are taken 24 hours before the study drug in neonates and up to 3-7 days before the study drug for older infants:

2.1. Biochemistry: Plasma creatinine, Na⁺, K⁺ Cl, AST, ALT, alkaline phosphatase, total bilirubin, conjugated bilirubin, albumin, total calcium, corrected calcium, magnesium, C-reactive protein.

2.2. Full blood count: Hgb, total white cell count, differential white cell count, MCV, MCH, MCHC and platelets.

2.3. Blood gas: pH, glucose, lactate, ionized calcium

3. In participants with urinary catheters in place the urine collection bag will be emptied immediately before the microdose is administered. Timed samples of urine will be collected for 48 hours after the microdose is administered.

4. DNA sampling will occur without any study specific blood samples. DNA will be obtained by one of the following methods depending on the clinical situation:

4.1. Buccal swab. A standard swab is placed in the child's mouth and brushed against the skin on the inside of the cheek. The cells are extracted and used to extract DNA.

4.2. Cell samples from clinically indicated samples. Samples sent to the laboratory for clinical purposes are retained for quality control purposes and usually discarded. These samples can be pooled and used to extract cells and DNA.

4.3. Dried blood spots. If there is excess blood left after the research assays it can be used to extract cells and DNA.

Intervention Type

Other

Phase

Not Applicable

Primary outcome(s)

The primary outcome of the study will be a noncompartmental model of midazolam disposition

Key secondary outcome(s)

The secondary outcome will be a population model of the whole dataset taking account of all the variables. Pharmacogenetic outcomes will relate continuous variables (midazolam or metabolism concentrations at steady state) with the presence of polymorphisms in CYP3A4

Completion date

31/12/2014

Eligibility**Key inclusion criteria**

1. Infants and toddlers from preterm neonates (32-36 GW at birth) up to 2 years
2. Having intravenous or intra-arterial access suitable for blood sampling
3. Written informed consent prior to any study-specific procedures
4. For dried blood spot sampling in addition to plasma, the participant must weigh more than 2.3 kg

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Child

Upper age limit

2 Years

Sex

All

Key exclusion criteria

1. History of allergy or hypersensitivity to midazolam
2. Serious hepatic and/or renal impairment defined as creatinine > 150 micromol or AST or ALT > 200
3. Be otherwise unsuitable for the study, in the opinion of the investigator
4. Extracorporeal membrane oxygenation (ECMO)
5. Haemofiltration, peritoneal dialysis, haemodialysis

Date of first enrolment

09/06/2014

Date of final enrolment

31/12/2014

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

Liverpool Women's NHS Foundation Trust

Liverpool

United Kingdom

L8 7SS

Sponsor information

Organisation

Liverpool Women's NHS Foundation Trust (UK)

ROR

<https://ror.org/04q5r0746>

Funder(s)

Funder type

Research organisation

Funder Name

ERA-NET PrioMedChild (Priority Medicines for Children) (Netherlands)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No