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Paediatric Accelerator Mass Spectrometry evaluation research study (midazolam)

Submission date
04/06/2014

Recruitment status
No longer recruiting

Registration date
23/06/2014

Overall study status
Completed

Last Edited
13/03/2017

Condition category
Other

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] 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 though 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

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
LWH0984

Study information

Scientific Title
A multi-centre clinical study to evaluate the use of a microtrace dose of 14C-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
14C-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

Study design
Multicentre observational open-label study

Primary study design
Observational

Secondary study design
Non randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Other

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

Secondary outcome measures
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

Overall study start date
09/06/2014

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

Age group
Child

Upper age limit
2 Years

Sex
Both

Target number of participants
25

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
England

United Kingdom

Study participating centre
Liverpool Women's NHS Foundation Trust
Liverpool
United Kingdom
L8 7SS

Sponsor information

Organisation
Liverpool Women's NHS Foundation Trust (UK)

Sponsor details
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Sponsor type

Hospital/treatment centre

Website
http://www.liverpoolwomens.nhs.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

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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