Clinical trial results:
Midazolam Measurement and Modelling using Matrix Samplers

Summary

EudraCT number	2014-004958-34
Trial protocol	GB
Global end of trial date	09 October 2016

Results information

Result version number	v1 (current)
This version publication date	05 August 2019
First version publication date	05 August 2019
Summary attachment (see zip file)	4Ms Study Summary (4Ms Study Summary.pdf)

Trial information

Trial identification

Sponsor protocol code	UNOLE0457

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Of Leicester
Sponsor organisation address	University Road , Leicester , United Kingdom, LE1 7RH
Public contact	Hitesh Pandya, University of Leicester, hp28@le.ac.uk
Scientific contact	Hitesh Pandya, University of Leicester, hp28@le.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 October 2016
Global end of trial reached?	Yes
Global end of trial date	09 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Main objective of the trial: To determine whether critically ill children metabolise midazolam differently to otherwise healthy children undergoing routine surgery.

Secondary objective of the trial: To determine whether blood midazolam level measurements made from micro-volume samples of dried blood are equivalent to blood midazolam measurements made using wet blood samples.

Protection of trial subjects:

NA

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	02 February 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 100
Worldwide total number of subjects	100
EEA total number of subjects	100

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	47
Children (2-11 years)	43
Adolescents (12-17 years)	10
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

NA

Pre-assignment

Screening details:

NA

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Overall Trial

Arm description:

Not applicable

Arm type	Experimental
Investigational medicinal product name	MIDAZOLAM
Investigational medicinal product code	SUB08950MIG
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous bolus use , Intravenous drip use

Dosage and administration details:

Dosage administered by the direct care team according to the local hospital policy

Number of subjects in period 1	Overall Trial
Started	100
Completed	100

Baseline characteristics

End points

End points reporting groups

Reporting group title	Overall Trial
Reporting group description: Not applicable	
Subject analysis set title	PICU Cohort
Subject analysis set type	Full analysis
Subject analysis set description: PICU Cohort	
Subject analysis set title	Surgical cohort
Subject analysis set type	Full analysis
Subject analysis set description: Surgical Cohort	

Primary: Midazolam Concentration

End point title	Midazolam Concentration[1]

End point description:

Primary end point(s): To determine midazolam pharmacokinetic (PK) parameters (clearance, volume of distribution and half-life) in critically ill children and in otherwise healthy children undergoing surgery.

Secondary end point(s): To determine whether measurement of midazolam levels using microvolume samples of dried blood is equivalent to midazolam measurements made using wet blood samples.

End point type	Primary

End point timeframe:

Duration of Trial

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was undertaken.

End point values	Overall Trial	PICU Cohort	Surgical cohort	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	100[2]	64[3]	36[4]	
Units: ng/ml				
arithmetic mean (full range (min-max))	188 (5 to 1987)	332 (5 to 1987)	28 (5 to 356)	

Notes:

[2] - All subjects

[3] - PICU Cohort

[4] - Surgical Cohort

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

All Safety Reporting was according to Sponsor (University of Leicester) processes, and as per the study protocol.

Adverse event reporting additional description:

Common adverse events and adverse effects occurring during the trial was expected, as a consequence of the underlying condition, or surgical procedures and therefore were not be recorded in the CRF or collected as a part of the study procedures.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	1

Frequency threshold for reporting non-serious adverse events: 1 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Common adverse events and adverse effects occurring during the trial were expected, as a consequence of the underlying condition, or surgical procedures and therefore were not be recorded in the CRF or collected as a part of the study procedures.
Any adverse events or adverse reactions that were experienced during the study period were dealt within a clinically relevant manner by the direct care team and details were recorded in the clinical notes where applicable.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

NA

Notes: