



## 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 <sup>[1]</sup>  |
| 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 <sup>[2]</sup> | 64 <sup>[3]</sup>    | 36 <sup>[4]</sup>    |  |
| 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<sup>[1]</sup>

---

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: