# Clinical trial results:
# Paramedic Analgesia Comparing Ketamine and MorphiNe in trauma

## Summary

| | |
|---|---|
| EudraCT number | 2020-000154-10 |
| Trial protocol | GB |
| Global end of trial date | 14 February 2025 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 02 March 2025 |
| First version publication date | 02 March 2025 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | SOC.12/19-20 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | ISRCTN14124474 |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | University of Warwick |
| Sponsor organisation address | Gibbett Hill Road, Coventry, United Kingdom, CV4 7AL |
| Public contact | Trial Manager, University of Warwick Clinical Trials Unit, 0247 6150478, packman@warwick.ac.uk |
| Scientific contact | Dr Michael Smyth, University of Warwick Clinical Trials Unit, 0247 6150478, packman@warwick.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 | 14 May 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 16 November 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 February 2025 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this trial is to determine whether paramedic administered ketamine or morphine provides more effective pain relief for patients reporting severe pain following trauma. This will be measured by using a 0-10 numeric rating scale and the Sum of Pain Intensity Difference (SPID).

Protection of trial subjects:

Procedures for emergency unblinding.
procedures in place to treat any distressing side effects e.g. abnormal behavioural reactions.
Options for rescue analgesia in the event trial analgesia was ineffective.
procedures in place for cases of accidental overdose
procedures in place for addressing non-disclosed pregnancy

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 20 October 2021 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 6 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United Kingdom: 449 |
| Worldwide total number of subjects | 449 |
| EEA total number of subjects | 0 |

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) | 0 |
| Children (2-11 years) | 0 |

| | |
|---|---|
| Adolescents (12-17 years) | 1 |
| Adults (18-64 years) | 202 |
| From 65 to 84 years | 155 |
| 85 years and over | 91 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Patients were eligible for inclusion if they had suffered an acute traumatic injury, were at least 16 years of age or over, reported a pain score of 7 or greater on a 0-10 numeric rating score (NRS) and, in the opinion of the attending paramedic, would normally require parenteral morphine for analgesia.

### Period 1

| | |
|---|---|
| Period 1 title | overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Blinding implementation details:

Treatment packs were manufactured and supplied by an appropriately licenced pharmaceutical company. Treatment packs, containing either ketamine or morphine, were identical in appearance, apart from their unique sequential number. Packs were distributed by the trial drug manufacturer to ensure equal proportions across participating sites. Individual participant randomisation occurred when the attending paramedic opened the trial treatment pack.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | morphine |

Arm description: -

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | morphine sulphate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intraosseous use, Intravenous use |

Dosage and administration details:

titrate to effect. maximum cummulative dose 20mg

| | |
|---|---|
| Investigational medicinal product name | ketamine hydrochloride |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intraosseous use, Intravenous use |

Dosage and administration details:

titrate to effect. maximum cummulative dose 30mg

| | |
|---|---|
| **Arm title** | ketamine |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | ketamine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intraosseous use, Intravenous use |

Dosage and administration details:
Titrate to effect. Maximum cummulative dose 30mg.

| **Number of subjects in period 1** | morphine | ketamine |
|---|---|---|
| Started | 230 | 219 |
| Completed | 230 | 219 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | morphine |
| Reporting group description: - | |
| Reporting group title | ketamine |
| Reporting group description: - | |

| Reporting group values | morphine | ketamine | Total |
|---|---|---|---|
| Number of subjects | 230 | 219 | 449 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 63.2 | 64.0 | |
| standard deviation | ± 22.1 | ± 21.3 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 124 | 117 | 241 |
| Male | 106 | 102 | 208 |

## End points

| End points reporting groups | |
|---|---|
| Reporting group title | morphine |
| Reporting group description: - | |
| Reporting group title | ketamine |
| Reporting group description: - | |

| Primary: SPID score | |
|---|---|
| End point title | SPID score |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| time from first drug administration to arrival at hospital | |

| End point values | morphine | ketamine | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 230 | 219 | | |
| Units: number | | | | |
| arithmetic mean (standard deviation) | 3.4 (± 3.0) | 3.5 (± 2.8) | | |

### Statistical analyses

| Statistical analysis title | Adjusted estimate |
|---|---|
| Comparison groups | morphine v ketamine |
| Number of subjects included in analysis | 449 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7 |
| Method | Regression, Linear |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.43 |
| upper limit | 0.64 |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: from administration of drug to 6 months post administration | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | CTCAE |
| Dictionary version | 5 |

| Reporting groups | |
|---|---|
| Reporting group title | morphine |
| Reporting group description: - | |
| Reporting group title | ketamine |
| Reporting group description: - | |

| Serious adverse events | morphine | ketamine | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 230 (1.74%) | 8 / 219 (3.65%) | |
| number of deaths (all causes) | 10 | 14 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Immediately life threatening problem | | | |
| subjects affected / exposed | 1 / 230 (0.43%) | 0 / 219 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 10 | 0 / 14 | |
| Prolonged hospitalisation | | | |
| subjects affected / exposed | 1 / 230 (0.43%) | 1 / 219 (0.46%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| subjects affected / exposed | 2 / 230 (0.87%) | 2 / 219 (0.91%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 10 | 0 / 14 | |
| Required medical intervention | | | |
| subjects affected / exposed | 4 / 230 (1.74%) | 1 / 219 (0.46%) | |
| occurrences causally related to treatment / all | 3 / 4 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 0.5 %

| **Non-serious adverse events** | morphine | ketamine | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 174 / 230 (75.65%) | 143 / 219 (65.30%) | |
| Injury, poisoning and procedural complications | | | |
| Other | Additional description: any non-serious adverse event not categorised as airway, respiratory, cardiovascular or nervous | | |
| subjects affected / exposed | 57 / 230 (24.78%) | 44 / 219 (20.09%) | |
| occurrences (all) | 57 | 44 | |
| Cardiac disorders | | | |
| Hypotension | Additional description: hypotension | | |
| subjects affected / exposed | 34 / 230 (14.78%) | 26 / 219 (11.87%) | |
| occurrences (all) | 34 | 26 | |
| Nervous system disorders | | | |
| Nervous system disorder | Additional description: altered consciousness or acute behavioural disturbance | | |
| subjects affected / exposed | 18 / 230 (7.83%) | 42 / 219 (19.18%) | |
| occurrences (all) | 18 | 42 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Airway | Additional description: need for any airway intervention e.g. positioning to ensure open airway, airway adjunct, suction | | |
| subjects affected / exposed | 27 / 230 (11.74%) | 16 / 219 (7.31%) | |
| occurrences (all) | 27 | 16 | |
| Hypoxia | Additional description: need for supplemental oxygen or assisted ventilation | | |
| subjects affected / exposed | 38 / 230 (16.52%) | 15 / 219 (6.85%) | |
| occurrences (all) | 38 | 15 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 22 December 2020 | Update to investigational medicinal product description to permit intraosseous administration |
| 14 April 2021 | Update to include risk assessment for concomitant use of a COVID-19 vaccine |
| 23 June 2021 | Revision to consent process. New and revised letters and consent forms |
| 30 June 2021 | Protocol amendment to correct dosing table. Minor update to eConsent forms |
| 25 October 2021 | Change of PI at Yorkshire site |
| 05 May 2022 | Update exclusion criteria and participant information sheet PIS |
| 04 October 2022 | Extension of trial recruitment whilst pending official extension. |
| 15 December 2022 | Extension of PACKMaN trial. |
| 04 October 2023 | Protocol amendment to update unblinding process and results letter for participants. Addition of final results letter for patients. |
| 25 October 2023 | Addition of participant unblinding letter |
| 17 November 2023 | Protocol amendment to update names of TSC PPI members |
| 25 January 2024 | Protocol amendment to provide clarity on who the hospital data collection form will be collected from and data retention where only verbal assent is in place. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---|---|---|
| 02 November 2020 | trial paused (before recruitment had commenced) due to cOVID-19 pandemic | 01 September 2021 |

Notes:

## Limitations and caveats

None reported