



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
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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 cumulative 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 cumulative 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 cumulative dose 30mg.

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

Baseline characteristics

Reporting groups

Reporting group title	morphine
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Reporting group description: -

Reporting group title	ketamine
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Reporting group description: -

Reporting group values	morphine	ketamine	Total
Number of subjects	230	219	449
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	63.2 ± 22.1	64.0 ± 21.3	-
Gender categorical 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
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	5
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Reporting groups

Reporting group title	morphine
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Reporting group description: -

Reporting group title	ketamine
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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