



Clinical trial results:

Improving understanding of Heroin Overdose Testing: diamorphine dose-escalation testing in a treated population

Summary

EudraCT number	2016-001877-34
Trial protocol	GB
Global end of trial date	11 March 2022

Results information

Result version number	v1 (current)
This version publication date	07 August 2025
First version publication date	07 August 2025
Summary attachment (see zip file)	CSR Hot-Treated (HOT-Treated-Clinical Study Report-final-signed.pdf)

Trial information

Trial identification

Sponsor protocol code	Hot-Treated
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	South London and Maudsley NHS Foundation Trust
Sponsor organisation address	Denmark Hill, London, United Kingdom, SE5 8AZ
Public contact	Professor John Strang, South London and Maudsley NHS Foundation Trust, 44 02078480438, john.strang@kcl.ac.uk
Scientific contact	Professor John Strang, South London and Maudsley NHS Foundation Trust, 44 02078480438, john.strang@kcl.ac.uk
Sponsor organisation name	King's College London
Sponsor organisation address	The Strand, London, United Kingdom, WC2R 2LS
Public contact	Professor John Strang, King's College London, 44 02078480438, john.strang@kcl.ac.uk
Scientific contact	Professor John Strang, King's College London, 44 02078480438, john.strang@kcl.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	26 November 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 March 2022
Global end of trial reached?	Yes
Global end of trial date	11 March 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate respiratory depression and hypoxaemic response to intravenous (IV) or intramuscular (IM) higher-than-regular doses of heroin as a marker for overdose

Protection of trial subjects:

Participants have the right to withdraw from the study at any time for any reason. The investigator also has the right to withdraw patients from the study drug in the event of inter-current illness, AEs, SAEs, SUSARs, protocol violations, cure, administrative reasons or other reasons. It is understood by all concerned that an excessive rate of withdrawals can render the study uninterpretable; therefore, unnecessary withdrawal of patients should be avoided. Should a patient decide to withdraw from the study, all efforts will be made to report the reason for withdrawal as thoroughly as possible and an assessment will be made by the clinical team as to whether follow-up is necessary (i.e. in case of any adverse events).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 April 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 4
Worldwide total number of subjects	4
EEA total number of subjects	4

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)	0
Adults (18-64 years)	4
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	5 ^[1]
Number of subjects completed	4

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 1
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Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: We do not count screened participants as enrolled.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Arm title	Diamorphine Hydrochloride BP
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Arm description:

Diamorphine is a narcotic analgesic which acts primarily on the central nervous system and smooth muscle. Diamorphine has a more rapid onset of activity than morphine as the first metabolite, monoacetylmorphine, more readily crosses the blood brain barrier.

Arm type	Active comparator
Investigational medicinal product name	Diamorphine Hydrochloride BP
Investigational medicinal product code	SUB13557MIG
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

100-500 mg per day
Intravenously

Number of subjects in period 1	Diamorphine Hydrochloride BP
Started	4
Completed	4

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial
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Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	4	4	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	3	3	
From 65-84 years	1	1	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	4	4	

End points

End points reporting groups

Reporting group title	Diamorphine Hydrochloride BP
Reporting group description: Diamorphine is a narcotic analgesic which acts primarily on the central nervous system and smooth muscle. Diamorphine has a more rapid onset of activity than morphine as the first metabolite, monoacetylmorphine, more readily crosses the blood brain barrier.	

Primary: Primary Endpoint - Blood Oxygen Saturation (SpO2)

End point title	Primary Endpoint - Blood Oxygen Saturation (SpO2) ^[1]
End point description:	

End point type	Primary
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End point timeframe:

All endpoints will be obtained by measurements taken during the study visits. (Trial lasting no longer than 9 months)

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: Please see uploaded report

End point values	Diamorphine Hydrochloride BP			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: SpO2 (%)				
arithmetic mean (standard deviation)	94.7 (± 1.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Primary Endpoint - End-Tidal Carbon Dioxide

End point title	Primary Endpoint - End-Tidal Carbon Dioxide ^[2]
End point description:	

End point type	Primary
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End point timeframe:

All endpoints will be obtained by measurements taken during the study visits. (Trial lasting no longer than 9 months)

Notes:

[2] - 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: Please see uploaded report

End point values	Diamorphine Hydrochloride BP			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: CO2 (%)				
arithmetic mean (standard deviation)	6.4 (± 0.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Primary Endpoint - Transcutaneous Carbon Dioxide

End point title	Primary Endpoint - Transcutaneous Carbon Dioxide ^[3]
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End point description:

End point type	Primary
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End point timeframe:

All endpoints will be obtained by measurements taken during the study visits. (Trial lasting no longer than 9 months)

Notes:

[3] - 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: Please see uploaded report

End point values	Diamorphine Hydrochloride BP			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: TcCO2 (%)				
arithmetic mean (standard deviation)	6.2 (± 0.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Primary Endpoint - Intercostal parasternal electromyography to measure neural respiratory drive

End point title	Primary Endpoint - Intercostal parasternal electromyography to measure neural respiratory drive ^[4]
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End point description:

End point type	Primary
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End point timeframe:

All endpoints will be obtained by measurements taken during the study visits. (Trial lasting no longer than 9 months)

Notes:

[4] - 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: Please see uploaded report

End point values	Diamorphine Hydrochloride BP			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: min-1				
arithmetic mean (standard deviation)	90.1 (± 27.3)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

14/08/2018 - 28/02/2024

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	Diamorphine
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Reporting group description: -

Serious adverse events	Diamorphine		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Diamorphine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)		
General disorders and administration site conditions			
Injection site irritation			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 August 2017	Protocol v1.3
25 May 2018	Protocol v1.4
13 March 2019	Protocol v1.5
20 September 2019	Protocol v1.6
26 March 2021	Protocol v1.7

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
20 March 2020	COVID-19 Pandemic	29 October 2021

Notes:

Limitations and caveats

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

The study was terminated prematurely because of the dwindling number of patients in the UK on diamorphine for their heroin addiction treatment and also because of a diamorphine shortage which affected the few patients who were on that treatment.

Notes: