Clinical trial results:
Bioavailability study of intranasal sufentanil/ketamine fixed combination in healthy volunteers

Summary

EudraCT number	2020-004488-14
Trial protocol	DK
Global end of trial date	02 June 2021

Results information

Result version number	v1 (current)
This version publication date	21 October 2022
First version publication date	21 October 2022
Summary attachment (see zip file)	PDC-01-0204 CSR synopsis (3834_CSR_2022_09_15-final-synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	PDC01-0204

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04807335
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cessatech AS
Sponsor organisation address	Kanonbådsvej 2, Copenhagen, Denmark, 1437
Public contact	CEO, Cessatech AS, jes.trygved@cessatech.com
Scientific contact	CEO, Cessatech AS, jes.trygved@cessatech.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001739-PIP02-16
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	15 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 June 2021
Global end of trial reached?	Yes
Global end of trial date	02 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the absolute bioavailability of intranasal sufentanil/ketamine in a standardized study set-up with healthy volunteers

Protection of trial subjects:

None

Background therapy:

None

Evidence for comparator:

The present study investigated bioavailability in a standardised set-up with adult healthy volunteers in accordance with the paediatric investigation plan approved by the European Medicines Agency for the development of a sufentanil/ketamine analgesic spray for treatment of acute pain in children (EMA_001739-PIP02-16)(1).
The primary objective for this PK study in adult healthy volunteers was to assess the biopharmaceutical performances (bioavailability) of the sufentanil/ketamine fixed combination compared to currently EU marketed intravenous ketamine and sufentanil products, allowing bridging to data for intravenous sufentanil and ketamine.

Actual start date of recruitment	17 March 2021
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	Denmark: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	15
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

15 subjects were included in the study at one site in Denmark during the period 17-Mar-2021 until 02-Jun-2021.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	15
Number of subjects completed	15

Period 1

Period 1 title	Treatment period 1
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not relevant, open study

Arms

Arm title	Ketamine IV

Arm description:

Intravenous (IV) ketamine 10 mg as a single bolus dose

Arm type	Active comparator
Investigational medicinal product name	Ketamine solution for injection, 50 mg/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Ketamine 10 mg as a single bolus dose

Number of subjects in period 1	Ketamine IV
Started	15
Completed	15

Period 2

Period 2 title	Treatment period 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not relevant, open study

Arms

Arm title	Sufentanil IV

Arm description:

Intravenous (IV) sufentanil 10 mcg as a single bolus dose

Arm type	Active comparator
Investigational medicinal product name	Sufentanil solution for injection, 5 mcg/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Sufentanil 10 mcg as a single bolus dose

Number of subjects in period 2[1]	Sufentanil IV
Started	14
Completed	14

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Cross over study

Period 3

Period 3 title	Treatment period 3
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not relevant, open study

Arms

Arm title	CT001

Arm description:

Sufentanil 27 mcg/ml + ketamine 27 mg/ml, nasal spray.

Arm type	Experimental

Investigational medicinal product name	Sufentanil 90 mcg/ml + ketamine 90 mg/ml, nasal spray.
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use

Dosage and administration details:

The nasal spray was administer 0.1 ml per spray. The administered intranasal dose was be 27 mcg sufentanil + 27 mg ketamine

Number of subjects in period 3	CT001
Started	14
Completed	14

Baseline characteristics

Reporting groups	
Reporting group title	Treatment period 1

Reporting group description: -

Reporting group values	Treatment period 1	Total	
Number of subjects	15	15	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	28.2		
standard deviation	± 6.0	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	15	15	

End points

End points reporting groups

Reporting group title	Ketamine IV
Reporting group description:	
Intravenous (IV) ketamine 10 mg as a single bolus dose	
Reporting group title	Sufentanil IV
Reporting group description:	
Intravenous (IV) sufentanil 10 mcg as a single bolus dose	
Reporting group title	CT001
Reporting group description:	
Sufentanil 27 mcg/ml + ketamine 27 mg/ml, nasal spray.	

Primary: Cmax Ketamine IV

End point title	Cmax Ketamine IV[1]
End point description:	

End point type	Primary
End point timeframe:	
One dosing	

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: Not applicable

End point values	Ketamine IV			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: mg/L				
geometric mean (geometric coefficient of variation)	0.0632 (± 60.0)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-t Ketamine IV

End point title	AUC0-t Ketamine IV[2]
End point description:	

End point type	Primary
End point timeframe:	
PK measured from dosing until 48 hours post dose	

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: Not applicable

End point values	Ketamine IV			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: mg/L*h				
geometric mean (geometric coefficient of variation)	0.0995 (± 20.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax Ketamine IN

End point title	Cmax Ketamine IN[3]

End point description:

End point type	Primary

End point timeframe:

PK was measured from dosing until 48 hours post dose

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: Not applicable

End point values	CT001			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: mg/L				
geometric mean (geometric coefficient of variation)	0.044 (± 39.9)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-t Ketamine IN

End point title	AUC0-t Ketamine IN[4]

End point description:

End point type	Primary

End point timeframe:

PK was measured form dosing until 48 hours post dose

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: Not applicable

End point values	CT001			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: mg/L*h				
geometric mean (geometric coefficient of variation)	0.131 (± 25.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax Sufentanil IV

End point title	Cmax Sufentanil IV[5]

End point description:

End point type	Primary

End point timeframe:

PK was measured from dosing until 48 hours post dose

Notes:

[5] - 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: Not applicable

End point values	Sufentanil IV			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: ug/L				
geometric mean (geometric coefficient of variation)	0.108 (± 86.7)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-t Sufentanil IV

End point title	AUC0-t Sufentanil IV[6]

End point description:

End point type	Primary

End point timeframe:

PK was measured from dosing until 48 hours post dose

Notes:

[6] - 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: Not applicable

End point values	Sufentanil IV			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: ug/L*h				
geometric mean (geometric coefficient of variation)	0119 (± 11.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax Sufentanil IN

End point title	Cmax Sufentanil IN[7]

End point description:

End point type	Primary

End point timeframe:

PK was measured from dosing until 48 hour post dose.

Notes:

[7] - 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: Not applicable

End point values	CT001			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: ug/L				
geometric mean (geometric coefficient of variation)	0.0342 (± 41.6)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-t Sufentanil IN

End point title	AUC0-t Sufentanil IN[8]

End point description:

End point type	Primary

End point timeframe:

PK was measured from dosing until 48 hours after dosing.

Notes:

[8] - 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: Not applicable

End point values	CT001			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: ug/L*h				
geometric mean (geometric coefficient of variation)	0.127 (± 26.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from first dose until 28 days after last dose.

Adverse event reporting additional description:

Adverse evets were collected based on study personnel observations during dosing and observation on site and spontaneous reporting from subjects.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Ketamine IV

Reporting group description:

Reporting events after treatment period were Ketamine IV was administered.

Reporting group title	Sufentanil IV

Reporting group description: -

Reporting group title	Sufentanil/Ketamine IN

Reporting group description: -

Serious adverse events	Ketamine IV	Sufentanil IV	Sufentanil/Ketamine IN
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Ketamine IV	Sufentanil IV	Sufentanil/Ketamine IN
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 15 (40.00%)	2 / 14 (14.29%)	4 / 14 (28.57%)
Injury, poisoning and procedural complications			
Nerve injury			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Headache			
subjects affected / exposed	2 / 15 (13.33%)	1 / 14 (7.14%)	2 / 14 (14.29%)
occurrences (all)	5	5	5
Dizziness			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 14 (0.00%)
occurrences (all)	1	1	1
Presyncope			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	1	1
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	1	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 15 (20.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	4	4	4
Psychiatric disorders			
Dissociation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	1	1

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

None reported