



Clinical trial results:

Analgesic Efficacy and Pharmacokinetic-pharmacodynamic Relationship of Intranasally Administered Sufentanil, Ketamine, and CT001 after Impacted Mandibular Third Molar Extraction

Summary

EudraCT number	2021-003258-21
Trial protocol	DK
Global end of trial date	05 October 2023

Results information

Result version number	v1 (current)
This version publication date	29 November 2024
First version publication date	29 November 2024

Trial information

Trial identification

Sponsor protocol code	PDC-01-0205
-----------------------	-------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05508594
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cessatech A/S
Sponsor organisation address	Strandvejen 60, Hellerup, Denmark, DK-2900
Public contact	CEO, Cessatech A/S, +45 93872309, info@cessatech.com
Scientific contact	CEO, Cessatech A/S, +45 93872309, info@cessatech.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-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	03 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 October 2023
Global end of trial reached?	Yes
Global end of trial date	05 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

-To investigate the postoperative analgesic efficacy of intranasal sufentanil, intranasal ketamine and intranasal CT001, in adults following impacted mandibular third molar extraction.

- To assess the relationship between analgesic efficacy and the plasma concentrations of intranasal sufentanil, intranasal ketamine and intranasal CT001.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki, adopted by the 18th World Medical Association (WMA) General Assembly, Helsinki, Finland, June 1964, and subsequent amendments and International Council for Harmonisation (ICH) guideline for Good Clinical Practice E6 (R2)(European Medicines Agency (EMA)/Committee for Medicinal Products for Human Use CHMP)/ICH/135/1995), including archiving of essential documents and the EU Clinical Trial Directive (CTD)2001/20/EC.

Background therapy:

None

Evidence for comparator:

Placebo is used as comparator.

Actual start date of recruitment	22 August 2023
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: 220
Worldwide total number of subjects	220
EEA total number of subjects	220

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	220
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted at a phase I unit in Denmark

Pre-assignment

Screening details:

Participants were referred to the phase I unit by dental clinics. The patients were randomised into the study if they reached a sufficient pain score within 5 hours after ending the dental procedure.

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Both the test product and comparators were colourless aqueous solutions with no smell, manufactured in identical nasal spray devices. No taste masking of the active product ingredients was performed, since the IMPs was administered as a nasal spray. The test product, active comparators and placebo were supplied to the site in packages containing the appropriate strengths to perform dosing according to the allocated treatment group.

PK samples were analysed by a central laboratory.

Arms

Are arms mutually exclusive?	Yes
Arm title	Sufentanil/ketamine (40mcg/40mg)

Arm description:

Participants received 2 doses of Sufentanil/ketamine (40mcg/40mg)-4 actuations of sufentanil/ketamine (9 mcg/9 mg) and 1 actuations of sufentanil/ketamine (4.5 mcg/4.5 mg) in both doses.

Arm type	Active comparator
Investigational medicinal product name	CT001 (9mcg/9mg)
Investigational medicinal product code	CT001 (9mcg/9mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use

Dosage and administration details:

Dose 100 ul in alternating nostrils

Investigational medicinal product name	CT001 (4.5mcg/4.5mg)
Investigational medicinal product code	CT001 (4.5mcg/4.5mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use

Dosage and administration details:

Dose 50 ul in alternating nostrils

Arm title	sufentanil/ketamine (27 mcg/27 mg)
------------------	------------------------------------

Arm description:

Participants received 2 doses of Sufentanil/ketamine (27mcg/27mg)- 3 actuations of sufentanil/ketamine (9 mcg/9 mg) and 2 actuations of placebo 50ul in both doses.

Arm type	Experimental
----------	--------------

Investigational medicinal product name	CT001 (9mcg/9mg)
Investigational medicinal product code	CT001 (9mcg/9mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 ul in alternating nostrils	
Arm title	sufentanil/ketamine (13 mcg/13 mg)
Arm description:	
Participants received 2 doses of Sufentanil/ketamine (13mcg/13mg)- 1 actuations of sufentanil/ketamine (9 mcg/9 mg), 1 actuations of sufentanil/ketamine (4.5 mcg/4.5 mg) and 3 actuations of placebo 100ul in both doses.	
Arm type	Experimental
Investigational medicinal product name	CT001 (9mcg/9mg)
Investigational medicinal product code	CT001 (9mcg/9mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Investigational medicinal product name	CT001 (4.5mcg/4.5mg)
Investigational medicinal product code	CT001 (4.5mcg/4.5mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 ul in alternating nostrils	
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 or 100 ul in alternating nostrils	
Arm title	sufentanil/ketamine (13 mcg/27 mg)
Arm description:	
Participants received 2 doses of Sufentanil/ketamine (13mcg/27mg)-1 actuations of sufentanil (9 mcg), 1 actuations of sufentanil (4.5 mcg) and 3 actuations of ketamin (9 mg) in both doses.	
Arm type	Experimental
Investigational medicinal product name	Sufentanil (9mcg)
Investigational medicinal product code	Sufentanil (9mcg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use

Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Investigational medicinal product name	Sufentanil (4.5mcg)
Investigational medicinal product code	Sufentanil (4.5mcg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 ul in alternating nostrils	
Investigational medicinal product name	Ketamin (9mg)
Investigational medicinal product code	Ketamin (9mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Arm title	sufentanil/ketamine (13 mcg/40 mg)
Arm description:	
Participants received 2 doses of Sufentanil/ketamine (13mcg/40mg)-1 actuations of sufentanil/ketamin (9 mcg/9mg), 1 actuations of sufentanil/ketamin (4.5 mcg/4.5 mg) and 3 actuations of ketamin (9 mg) in both doses.	
Arm type	Experimental
Investigational medicinal product name	CT001 (9mcg/9mg)
Investigational medicinal product code	CT001 (9mcg/9mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Investigational medicinal product name	CT001 (4.5mcg/4.5mg)
Investigational medicinal product code	CT001 (4.5mcg/4.5mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 ul in alternating nostrils	
Investigational medicinal product name	Ketamin (9mg)
Investigational medicinal product code	Ketamin (9mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Arm title	sufentanil/ketamine (27 mcg/13 mg)
Arm description:	
Participants received 2 doses of Sufentanil/ketamine (27 mcg/13mg)-3 actuations of sufentanil (9 mcg), 1 actuations of ketamin (9 mg) and 1 actuations of ketamin (4.5 mcg) in both doses.	
Arm type	Experimental

Investigational medicinal product name	CT001 (9mcg/9mg)
Investigational medicinal product code	CT001 (9mcg/9mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Investigational medicinal product name	CT001 (4.5mcg/4.5mg)
Investigational medicinal product code	CT001 (4.5mcg/4.5mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 ul in alternating nostrils	
Investigational medicinal product name	Sufentanil (9mcg)
Investigational medicinal product code	Sufentanil (9mcg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Arm title	sufentanil/ketamine (27 mcg/40 mg)
Arm description:	
Participants received 2 doses of Sufentanil/ketamine (27mcg/40mg)-3 actuations of sufentanil/ketamin (9 mcg/9mg), 1 actuations of sufentanil (9 mcg) and 1 actuations of sufentanil (4.5 mcg) in both doses.	
Arm type	Experimental
Investigational medicinal product name	CT001 (9mcg/9mg)
Investigational medicinal product code	CT001 (9mcg/9mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Investigational medicinal product name	Sufentanil (9mcg)
Investigational medicinal product code	Sufentanil (9mcg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Investigational medicinal product name	Sufentanil (4.5mcg)
Investigational medicinal product code	Sufentanil (4.5mcg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 ul in alternating nostrils	
Arm title	Sufentnail (40 mcg)
Arm description:	
Participants received 2 doses of Sufentanil (40mcg)-4 actuations of sufentanil (9 mcg) and 1 sufentanil (4.5 mcg) in both doses.	
Arm type	Experimental

Investigational medicinal product name	Sufentanil (9mcg)
Investigational medicinal product code	Sufentanil (9mcg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Investigational medicinal product name	Sufentanil (4.5mcg)
Investigational medicinal product code	Sufentanil (4.5mcg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 ul in alternating nostrils	
Arm title	Sufentanil (27 mcg)
Arm description:	
Participants received 2 doses of Sufentanil (27mcg)-3 actuations of sufentanil (9 mcg/9 mg) and 2 actuations of placebo 50ul in both doses.	
Arm type	Experimental
Investigational medicinal product name	Sufentanil (9mcg)
Investigational medicinal product code	Sufentanil (9mcg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 or 100 ul in alternating nostrils	
Arm title	Sufentanil (13 mcg)
Arm description:	
Participants received 2 doses of Sufentanil (13 mcg)-3 actuations of sufentanil/ketamine (9 mcg/9 mg) and 2 actuations of placebo 50ul in both doses.	
Arm type	Experimental
Investigational medicinal product name	Sufentanil (9mcg)
Investigational medicinal product code	Sufentanil (9mcg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 or 100 ul in alternating nostrils	

Arm title	Ketamin (40 mg)
Arm description: Participants received 2 doses of Ketamine (40mg)-3 actuations of ketamine (9 mg) and 2 actuations of placebo 50ul in both doses.	
Arm type	Experimental
Investigational medicinal product name	Ketamin (9mg)
Investigational medicinal product code	Ketamin (9mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details: Dose 100 ul in alternating nostrils	
Investigational medicinal product name	Ketamin (4.5mg)
Investigational medicinal product code	Ketamin (4.5mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details: Dose 50 ul in alternating nostrils	
Arm title	Ketamin (27 mg)
Arm description: Participants received 2 doses of Ketamine (27 mg)-3 actuations of ketamin (9 mg) and 2 actuations of placebo 50ul in both doses.	
Arm type	Experimental
Investigational medicinal product name	Ketamin (9mg)
Investigational medicinal product code	Ketamin (9mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details: Dose 100 ul in alternating nostrils	
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details: Dose 50 or 100 ul in alternating nostrils	
Arm title	Ketamin (13 mg)
Arm description: Participants received 2 doses of Ketamine (13 mg)-3 actuations of sufentanil/ketamine (9 mcg/9 mg) and 2 actuations of placebo 50ul in both doses.	
Arm type	Experimental
Investigational medicinal product name	Ketamin (9mg)
Investigational medicinal product code	Ketamin (9mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details: Dose 100 ul in alternating nostrils	

Investigational medicinal product name	Ketamin (4.5mg)
Investigational medicinal product code	Ketamin (4.5mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 ul in alternating nostrils	
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 or 100 ul in alternating nostrils	
Arm title	Placebo
Arm description:	
Participants received 2 doses of Placebo	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 or 100 ul in alternating nostrils	
Arm title	sufentanil/ketamine (40 mcg/13 mg)
Arm description:	
Participants received 2 doses of Sufentanil/ketamine (40mcg/13 mg)-1 actuations of sufentanil/ketamine (9 mcg/9 mg), 1 actuations of sufentanil/ketamine (4.5 mcg/4.5 mg) and 1 actuations of sufentanil (9 mcg) in both doses.	
Arm type	Experimental
Investigational medicinal product name	CT001 (9mcg/9mg)
Investigational medicinal product code	CT001 (9mcg/9mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Investigational medicinal product name	CT001 (4.5mcg/4.5mg)
Investigational medicinal product code	CT001 (4.5mcg/4.5mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 ul in alternating nostrils	
Investigational medicinal product name	Sufentanil (9mcg)
Investigational medicinal product code	Sufentanil (9mcg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	

Arm title	sufentanil/ketamine (40 mcg/27 mg)
Arm description:	
Participants received 2 doses of Sufentanil/ketamine (40mcg/27mg)-3 actuations of sufentanil/ketamine (9 mcg/9 mg) and 1 actuations sufentanil (9 mcg) and sufentanil (4.5 mcg) in both doses.	
Arm type	Experimental
Investigational medicinal product name	CT001 (9mcg/9mg)
Investigational medicinal product code	CT001 (9mcg/9mg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Investigational medicinal product name	Sufentanil (9mcg)
Investigational medicinal product code	Sufentanil (9mcg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 100 ul in alternating nostrils	
Investigational medicinal product name	Sufentanil (4.5mcg)
Investigational medicinal product code	Sufentanil (4.5mcg)
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use
Dosage and administration details:	
Dose 50 ul in alternating nostrils	

Number of subjects in period 1	Sufentanil/ketamine (40mcg/40mg)	sufentanil/ketamine (27 mcg/27 mg)	sufentanil/ketamine (13 mcg/13 mg)
Started	5	40	5
Completed	5	40	5

Number of subjects in period 1	sufentanil/ketamine (13 mcg/27 mg)	sufentanil/ketamine (13 mcg/40 mg)	sufentanil/ketamine (27 mcg/13 mg)
Started	5	5	5
Completed	5	5	5

Number of subjects in period 1	sufentanil/ketamine (27 mcg/40 mg)	Sufentnail (40 mcg)	Sufentanil (27 mcg)
Started	5	5	40
Completed	5	5	40

Number of subjects in period 1	Sufentanil (13 mcg)	Ketamin (40 mg)	Ketamin (27 mg)
Started	5	5	40
Completed	5	5	40

Number of subjects in period 1	Ketamin (13 mg)	Placebo	sufentanil/ketamine (40 mcg/13 mg)
Started	5	40	5
Completed	5	40	5

Number of subjects in period 1	sufentanil/ketamine (40 mcg/27 mg)
Started	5
Completed	5

End points

End points reporting groups

Reporting group title	Sufentanil/ketamine (40mcg/40mg)
Reporting group description: Participants received 2 doses of Sufentanil/ketamine (40mcg/40mg)-4 actuations of sufentanil/ketamine (9 mcg/9 mg) and 1 actuations of sufentanil/ketamine (4.5 mcg/4.5 mg) in both doses.	
Reporting group title	sufentanil/ketamine (27 mcg/27 mg)
Reporting group description: Participants received 2 doses of Sufentanil/ketamine (27mcg/27mg)- 3 actuations of sufentanil/ketamine (9 mcg/9 mg) and 2 actuations of placebo 50ul in both doses.	
Reporting group title	sufentanil/ketamine (13 mcg/13 mg)
Reporting group description: Participants received 2 doses of Sufentanil/ketamine (13mcg/13mg)- 1 actuations of sufentanil/ketamine (9 mcg/9 mg), 1 actuations of sufentanil/ketamine (4.5 mcg/4.5 mg) and 3 actuations of placebo 100ul in both doses.	
Reporting group title	sufentanil/ketamine (13 mcg/27 mg)
Reporting group description: Participants received 2 doses of Sufentanil/ketamine (13mcg/27mg)-1 actuations of sufentanil (9 mcg), 1 actuations of sufentanil (4.5 mcg) and 3 actuations of ketamin (9 mg) in both doses.	
Reporting group title	sufentanil/ketamine (13 mcg/40 mg)
Reporting group description: Participants received 2 doses of Sufentanil/ketamine (13mcg/40mg)-1 actuations of sufentanil/ketamin (9 mcg/9mg), 1 actuations of sufentanil/ketamin (4.5 mcg/4.5 mg) and 3 actuations of ketamin (9 mg) in both doses.	
Reporting group title	sufentanil/ketamine (27 mcg/13 mg)
Reporting group description: Participants received 2 doses of Sufentanil/ketamine (27 mcg/13mg)-3 actuations of sufentanil (9 mcg), 1 actuations of ketamin (9 mg) and 1 actuations of ketamin (4.5 mcg) in both doses.	
Reporting group title	sufentanil/ketamine (27 mcg/40 mg)
Reporting group description: Participants received 2 doses of Sufentanil/ketamine (27mcg/40mg)-3 actuations of sufentanil/ketamin (9 mcg/9mg), 1 actuations of sufentanil (9 mcg) and 1 actuations of sufentanil (4.5 mcg) in both doses.	
Reporting group title	Sufentnail (40 mcg)
Reporting group description: Participants received 2 doses of Sufentanil (40mcg)-4 actuations of sufentanil (9 mcg) and 1 sufentanil (4.5 mcg) in both doses.	
Reporting group title	Sufentanil (27 mcg)
Reporting group description: Participants received 2 doses of Sufentanil (27mcg)-3 actuations of sufentanil (9 mcg/9 mg) and 2 actuations of placebo 50ul in both doses.	
Reporting group title	Sufentanil (13 mcg)
Reporting group description: Participants received 2 doses of Sufentanil (13 mcg)-3 actuations of sufentanil/ketamine (9 mcg/9 mg) and 2 actuations of placebo 50ul in both doses.	
Reporting group title	Ketamin (40 mg)
Reporting group description: Participants received 2 doses of Ketamine (40mg)-3 actuations of ketamine (9 mg) and 2 actuations of placebo 50ul in both doses.	
Reporting group title	Ketamin (27 mg)
Reporting group description: Participants received 2 doses of Ketamine (27 mg)-3 actuations of ketamin (9 mg) and 2 actuations of placebo 50ul in both doses.	
Reporting group title	Ketamin (13 mg)

Reporting group description:

Participants received 2 doses of Ketamine (13 mg)-3 actuations of sufentanil/ketamine (9 mcg/9 mg) and 2 actuations of placebo 50ul in both doses.

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

Participants received 2 doses of Placebo

Reporting group title	sufentanil/ketamine (40 mcg/13 mg)
-----------------------	------------------------------------

Reporting group description:

Participants received 2 doses of Sufentanil/ketamine (40mcg/13 mg)-1 actuations of sufentanil/ketamine (9 mcg/9 mg), 1 actuations of sufentanil/ketamine (4.5 mcg/4.5 mg) and 1 actuations of sufentanil (9 mcg) in both doses.

Reporting group title	sufentanil/ketamine (40 mcg/27 mg)
-----------------------	------------------------------------

Reporting group description:

Participants received 2 doses of Sufentanil/ketamine (40mcg/27mg)-3 actuations of sufentanil/ketamine (9 mcg/9 mg) and 1 actuations sufentanil (9 mcg) and sufentanil (4.5 mcg) in both doses.

Subject analysis set title	Safety Population
----------------------------	-------------------

Subject analysis set type	Safety analysis
---------------------------	-----------------

Subject analysis set description:

The Safety Population includes all randomised participants who received at least one dose of study treatment. Participants will be analysed according to the study treatment received, where treatment received is defined as the first study medication received.

Primary: Primary Endpoint - Sum pain intensity difference (SPID) at 55 min

End point title	Primary Endpoint - Sum pain intensity difference (SPID) at 55 min ^[1]
-----------------	--

End point description:

Sum of Pain intensity difference (SPID) at 55 min

End point type	Primary
----------------	---------

End point timeframe:

Measure at 55 min after 1st dose

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms were included in the analysis of the primary endpoint

End point values	sufentanil/ketamine (27 mcg/27 mg)	Sufentanil (27 mcg)	Ketamin (27 mg)	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	40	40	40 ^[2]
Units: SPID				
least squares mean (confidence interval 95%)	-13.59 (-16.58 to -10.60)	-17.20 (-20.19 to -14.21)	-5.90 (-8.90 to -2.90)	-1.00 (-4.11 to 2.10)

Notes:

[2] - 40

Statistical analyses

Statistical analysis title	Primary endpoint
Comparison groups	Placebo v sufentanil/ketamine (27 mcg/27 mg)

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-12.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.89
upper limit	-8.28

Statistical analysis title	Primary endpoint
Comparison groups	sufentanil/ketamine (27 mcg/27 mg) v Ketamin (27 mg)
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-7.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.92
upper limit	-3.46

Statistical analysis title	Primary endpoint
Comparison groups	sufentanil/ketamine (27 mcg/27 mg) v Sufentanil (27 mcg)
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.094
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	7.84

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events were collected in the study. Collection period from first dose until visit 4 (Day 10 to 14).

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	CT001 (sufentanil/ketmain 27 mcg/27 mg)
Reporting group description:	
Sufentanil/ketamin (27mcg/27mg)	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Ketamin (27 mg)
Reporting group description: -	
Reporting group title	Sufentanil (27 mcg)
Reporting group description: -	
Reporting group title	Other Ketamin groups
Reporting group description: -	
Reporting group title	Other Sufentanil groups
Reporting group description: -	
Reporting group title	Other Sufentanil/ketamin groups
Reporting group description: -	

Serious adverse events	CT001 (sufentanil/ketmain 27 mcg/27 mg)	Placebo	Ketamin (27 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	0 / 40 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			

subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Sufentanil (27 mcg)	Other Ketamin groups	Other Sufentanil groups
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 40 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Other Sufentanil/ketamin groups		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	CT001 (sufentanil/ketmain 27 mcg/27 mg)	Placebo	Ketamin (27 mg)
Total subjects affected by non-serious adverse events subjects affected / exposed	36 / 40 (90.00%)	22 / 40 (55.00%)	33 / 40 (82.50%)
Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all)	8 / 40 (20.00%) 8	9 / 40 (22.50%) 9	9 / 40 (22.50%) 9
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 40 (0.00%) 0	2 / 40 (5.00%) 2
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all)	24 / 40 (60.00%) 31 5 / 40 (12.50%) 5 1 / 40 (2.50%) 1	3 / 40 (7.50%) 9 4 / 40 (10.00%) 4 0 / 40 (0.00%) 0	20 / 40 (50.00%) 21 3 / 40 (7.50%) 3 0 / 40 (0.00%) 0
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Feeling abnormal subjects affected / exposed occurrences (all)	18 / 40 (45.00%) 19 10 / 40 (25.00%) 10	4 / 40 (10.00%) 4 0 / 40 (0.00%) 0	8 / 40 (20.00%) 8 4 / 40 (10.00%) 4
Ear and labyrinth disorders			

Ear discomfort subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 40 (0.00%) 0	2 / 40 (5.00%) 2
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	0 / 40 (0.00%) 0	0 / 40 (0.00%) 1
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	20 / 40 (50.00%) 23 4 / 40 (10.00%) 5	1 / 40 (2.50%) 1 0 / 40 (0.00%) 0	3 / 40 (7.50%) 3 0 / 40 (0.00%) 0
Skin and subcutaneous tissue disorders Hyperhidrosis subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3 0 / 40 (0.00%) 0	0 / 40 (0.00%) 0 0 / 40 (0.00%) 0	1 / 40 (2.50%) 1 0 / 40 (0.00%) 0
Infections and infestations Post procedural infection subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1 0 / 40 (0.00%) 0	1 / 40 (2.50%) 1 2 / 40 (5.00%) 2	1 / 40 (2.50%) 1 0 / 40 (0.00%) 0

Non-serious adverse events	Sufentanil (27 mcg)	Other Ketamin groups	Other Sufentanil groups
Total subjects affected by non-serious adverse events subjects affected / exposed	38 / 40 (95.00%)	5 / 10 (50.00%)	9 / 10 (90.00%)
Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all)	16 / 40 (40.00%) 16	1 / 10 (10.00%) 1	3 / 10 (30.00%) 3
Cardiac disorders			

Palpitations subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	33 / 40 (82.50%) 39	1 / 10 (10.00%) 1	5 / 10 (50.00%) 6
Headache subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Paraesthesia subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	25 / 40 (62.50%) 26	0 / 10 (0.00%) 0	4 / 10 (40.00%) 4
Feeling abnormal subjects affected / exposed occurrences (all)	6 / 40 (15.00%) 6	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Ear and labyrinth disorders Ear discomfort subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	26 / 40 (65.00%) 30	2 / 10 (20.00%) 2	5 / 10 (50.00%) 5
Vomiting subjects affected / exposed occurrences (all)	8 / 40 (20.00%) 12	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Skin and subcutaneous tissue disorders			

Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Infections and infestations Post procedural infection subjects affected / exposed occurrences (all)	4 / 40 (10.00%) 4	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Pharyngitis subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0

Non-serious adverse events	Other Sufentanil/ketamin groups		
Total subjects affected by non-serious adverse events subjects affected / exposed	35 / 40 (87.50%)		
Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all)	10 / 40 (25.00%) 10		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	23 / 40 (57.50%) 27		
Headache subjects affected / exposed occurrences (all)	4 / 40 (10.00%) 4		
Paraesthesia subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
General disorders and administration site conditions			

<p>Fatigue</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>22 / 40 (55.00%)</p> <p>23</p>		
<p>Feeling abnormal</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>8 / 40 (20.00%)</p> <p>8</p>		
<p>Ear and labyrinth disorders</p> <p>Ear discomfort</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 40 (5.00%)</p> <p>2</p>		
<p>Eye disorders</p> <p>Vision blurred</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 40 (0.00%)</p> <p>0</p>		
<p>Gastrointestinal disorders</p> <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>17 / 40 (42.50%)</p> <p>18</p> <p>9 / 40 (22.50%)</p> <p>10</p>		
<p>Skin and subcutaneous tissue disorders</p> <p>Hyperhidrosis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pruritus</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 40 (5.00%)</p> <p>2</p> <p>0 / 40 (0.00%)</p> <p>0</p>		
<p>Infections and infestations</p> <p>Post procedural infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 40 (7.50%)</p> <p>3</p> <p>0 / 40 (0.00%)</p> <p>0</p>		

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.

None

Notes: