Clinical trial results:
An Open-label, 8-Week Study to Compare the Comfort and Ease of Use of Five Different Treatment Regimens for CNTX-4975-05 Intra-articular Injection in Subjects with Chronic, Moderate-to-Severe Osteoarthritis Knee Pain

Summary

EudraCT number	2018-003094-10
Trial protocol	GB DE ES
Global end of trial date	17 October 2019

Results information

Result version number	v1 (current)
This version publication date	27 January 2021
First version publication date	27 January 2021

Trial information

Trial identification

Sponsor protocol code	CNTX-4975i-OA-303

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03661996
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Centrexion Therapeutics Corp
Sponsor organisation address	200 State Street, 6th Floor, Boston , United States,
Public contact	Kimberley Guedes, Centrexion Therapeutics Corp, +1 6178376920, kguedes@centrexion.com
Scientific contact	Kimberley Guedes, Centrexion Therapeutics Corp, +1 6178376920, kguedes@centrexion.com

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	Interim
Date of interim/final analysis	17 October 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 October 2019
Global end of trial reached?	Yes
Global end of trial date	17 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to determine the optimal procedures for administering CNTX-4975-05 as a single IA injection into knee(s) with OA, balancing comfort and ease of use of methods of cooling and administration.

Protection of trial subjects:

Ethics Committee Approval

Background therapy:

Subjects were able to enroll into the study with a single analgesic of their choice for their OA knee pain. (prescription or OTC).

Evidence for comparator:

This was an open-label study. No comparators were used in this trial.

Actual start date of recruitment	28 September 2018
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	Spain: 74
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Germany: 97
Country: Number of subjects enrolled	United States: 668
Worldwide total number of subjects	848
EEA total number of subjects	180

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)	458
From 65 to 84 years	384
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

recruitment period for Germany, Spain and United Kingdom: 31 January 2019 to 17 October 2019

Screening Period was up to 15 days

Pre-assignment

Screening details:

Number of subjects Screened by Country:
- United Kingdom = 16
- Spain = 93
- Germany = 106
- United States = 1189
- Total Screened = 1404

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

open label study

Arms

Are arms mutually exclusive?	Yes
Arm title	Breg Cooling solution

Arm description:

Joint cooling was provided by a cooling wrap with an ice water pump system (Breg Cooler). Cooling was applied 15 minutes prior to IA injection of 15 mL 2% lidocaine (without epinephrine) into the knee. Cooling was resumed for a further 30-minutes prior to the IA injection of CNTX-4975-05 using a separate syringe and needle. Controlled cooling could then be reapplied for 30-90 minutes post-injection.

Arm type	control group
Investigational medicinal product name	Capsaicin 1mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

1mg CNTX-4975-05 on day 1

Arm title	Gel Pack Cooling

Arm description:

Joint cooling was provided by a Gel pack applied for 40 -minutes prior to injection of 2% lidocaine (without epinephrine) into the knee. Cooling was resumed for a further 10-minutes prior to the IA injection of CNTX-4975-05 using a separate syringe and needle. Controlled cooling could then be reapplied for 10-90 minutes post-injection.

Arm type	Experimental
Investigational medicinal product name	Capsaicin 1mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

1mg CNTX-4975-05 on day 1

Arm title	Shortened Gel Pack Cooling

Arm description:

Joint cooling was provided by a Gel pack applied for 30 -minutes prior to injection of 2% lidocaine (without epinephrine) into the knee. Cooling was resumed for a further 5-minutes prior to the IA injection of CNTX-4975-05 using a separate syringe and needle. Controlled cooling could then be reapplied for up to 90 minutes post-injection.

Arm type	Experimental
Investigational medicinal product name	Capsaicin 1mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

1mg CNTX-4975-05 on day 1

Arm title	Single Needle Injection, Gel Pack Cooling, 2% Lidocaine

Arm description:

Joint cooling was provided by a Gel pack applied for 45 minutes prior to injection of 2% lidocaine (without epinephrine) into the knee. An IA injection of CNTX-4975-05 using the same needle followed immediately after the 2% lidocaine injection. Controlled cooling could then be reapplied for up to 90 minutes post-injection.

Arm type	Experimental
Investigational medicinal product name	Capsaicin 1mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

1mg CNTX-4975-05 on day 1

Arm title	Single Needle Injection, Gel Pack Cooling, 1% Lidocaine

Arm description:

Joint cooling was provided by a Gel pack applied for 45 -minutes prior to injection of 1% lidocaine (without epinephrine) into the knee. An IA injection of CNTX-4975-05 using the same needle followed immediately after the 1% lidocaine injection. Gel pack cooling could then be reapplied for up to 90 minutes post-injection.

Arm type	Experimental
Investigational medicinal product name	Capsaicin 1mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

1mg CNTX-4975-05 on day 1

Number of subjects in period 1	Breg Cooling solution	Gel Pack Cooling	Shortened Gel Pack Cooling
Started	162	179	175
Completed	150	172	170
Not completed	12	7	5
Consent withdrawn by subject	3	5	1
Physician decision	1	1	1
Adverse event, non-fatal	-	-	1
study terminated by sponsor	2	-	-
Lost to follow-up	5	1	2
not specified	1	-	-
Protocol deviation	-	-	-

Number of subjects in period 1	Single Needle Injection, Gel Pack Cooling, 2% Lidocaine	Single Needle Injection, Gel Pack Cooling, 1% Lidocaine
Started	160	172
Completed	150	159
Not completed	10	13
Consent withdrawn by subject	7	6
Physician decision	-	-
Adverse event, non-fatal	1	-
study terminated by sponsor	-	-
Lost to follow-up	2	6
not specified	-	-
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	848	848	
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)	458	458	
From 65-84 years	384	384	
85 years and over	6	6	
Gender categorical Units: Subjects			
Female	508	508	
Male	340	340	

End points

End points reporting groups

Reporting group title	Breg Cooling solution

Reporting group description:

Joint cooling was provided by a cooling wrap with an ice water pump system (Breg Cooler). Cooling was applied 15 minutes prior to IA injection of 15 mL 2% lidocaine (without epinephrine) into the knee. Cooling was resumed for a further 30-minutes prior to the IA injection of CNTX-4975-05 using a separate syringe and needle. Controlled cooling could then be reapplied for 30-90 minutes post-injection.

Reporting group title	Gel Pack Cooling

Reporting group description:

Joint cooling was provided by a Gel pack applied for 40 -minutes prior to injection of 2% lidocaine (without epinephrine) into the knee. Cooling was resumed for a further 10-minutes prior to the IA injection of CNTX-4975-05 using a separate syringe and needle. Controlled cooling could then be reapplied for 10-90 minutes post-injection.

Reporting group title	Shortened Gel Pack Cooling

Reporting group description:

Joint cooling was provided by a Gel pack applied for 30 -minutes prior to injection of 2% lidocaine (without epinephrine) into the knee. Cooling was resumed for a further 5-minutes prior to the IA injection of CNTX-4975-05 using a separate syringe and needle. Controlled cooling could then be reapplied for up to 90 minutes post-injection.

Reporting group title	Single Needle Injection, Gel Pack Cooling, 2% Lidocaine

Reporting group description:

Joint cooling was provided by a Gel pack applied for 45 minutes prior to injection of 2% lidocaine (without epinephrine) into the knee. An IA injection of CNTX-4975-05 using the same needle followed immediately after the 2% lidocaine injection. Controlled cooling could then be reapplied for up to 90 minutes post-injection.

Reporting group title	Single Needle Injection, Gel Pack Cooling, 1% Lidocaine

Reporting group description:

Joint cooling was provided by a Gel pack applied for 45 -minutes prior to injection of 1% lidocaine (without epinephrine) into the knee. An IA injection of CNTX-4975-05 using the same needle followed immediately after the 1% lidocaine injection. Gel pack cooling could then be reapplied for up to 90 minutes post-injection.

Primary: assessment of the CNTX-4975-05 joint treatment regimens, with the Breg Cooling Control Group as the control, using a combination of 3 assessments of the index knee.

End point title	assessment of the CNTX-4975-05 joint treatment regimens, with the Breg Cooling Control Group as the control, using a combination of 3 assessments of the index knee.[1]

End point description:

The primary efficacy endpoint was a composite measure assessing pain after injection and subject and investigator satisfaction with the treatment regimen.
Secondary measures included:
1. Assessment of the composite measure in the non-index knee.
2. OMERACT-OARSI Responders at Week 8

End point type	Primary

End point timeframe:

Day 3, week 4, week 8

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: The primary analysis, performed on the ITT population, compared each experimental

treatment regimen with the Breg Cooling Control Group calculated from the following3measures:1)pain 30 minutes after CNTX-4975-05 injection (using the following 5-point scale: 0 [none],1 [mild],2 [moderate],3 [moderately severe],and4[severe]),2)SS with the treatment regimen;and3)IS with the treatment regimen,all assessed on the index knee.
Allsecondary efficacyendpoints were summarized using descriptive statistics

End point values	Breg Cooling solution	Gel Pack Cooling	Shortened Gel Pack Cooling	Single Needle Injection, Gel Pack Cooling, 2% Lidocaine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	162	179	175	160
Units: pain measurement scale				
number (not applicable)	150	172	170	150

End point values	Single Needle Injection, Gel Pack Cooling, 1% Lidocaine			
Subject group type	Reporting group			
Number of subjects analysed	172			
Units: pain measurement scale				
number (not applicable)	159			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

During clinical trial

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19

Reporting groups

Reporting group title	overall trial

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Treatment emergent AEs were reported in 22% of subjects; < 1% of the subjects experienced TEAEs that were serious. The TEAEs occurring in > 2% of subjects were procedural pain (2.9%), arthralgia (2.2%), and nausea (2.1%), with no meaningful differences between treatment groups.

Serious adverse events	overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 848 (0.71%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	6 / 848 (0.71%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 848 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity	Additional description: Due to the temporal relationship between IA injection and SAE, the Investigator considered this event of hypersensitivity to be "possibly related" to study drug.		
subjects affected / exposed	1 / 848 (0.12%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			

subjects affected / exposed	1 / 848 (0.12%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 848 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	1 / 848 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 848 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 August 2019	This amendment was to update the protocol and IB with a reported serious adverse event. The amendment was to inform investigators that acute allergic/hypersensitivity reactions are an identified risk following CNTX-4975 treatment. investigators should ensure subjects are observed for 30 minutes post-IA injection to ensure appropriate management should an allergic reaction occur. A new section was included in the protocol to highlight the hypersensitivity reaction as an adverse event of special interest. The reference safety information section was updated in the IB

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
08 May 2019	The trial was briefly paused (08 May-13 June 2019) following the single event of acute allergic reaction (hypersensitivity) to allow for a clinical evaluation of the risk, to inform the study sites and the ethics committees of the event, and to allow for clinical sites to add additional safety equipment per the FDA.	13 June 2019

Notes:

Limitations and caveats

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

none

Notes: