Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study in Parkinson's Disease Patients With Moderate to Severe Dyskinesia to Assess the Efficacy and Safety/Tolerability of Two Dose Combinations Of JM-010

Summary

EudraCT number	2017-003415-19
Trial protocol	ES IT SK
Global end of trial date	21 March 2024

Results information

Result version number	v1 (current)
This version publication date	16 November 2024
First version publication date	16 November 2024

Trial information

Trial identification

Sponsor protocol code	JM-010CS03

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Contera Pharma A/S
Sponsor organisation address	DTU Science Park, Venlighedsvej 4, Hørsholm, Denmark, 2970
Public contact	Clinical Trials Information, Contera Pharma A/S, +34 900834223, RegistroEspanolDeEstudiosClinicos@druginfo.com
Scientific contact	Clinical Trials Information, Contera Pharma A/S, +34 900834223, RegistroEspanolDeEstudiosClinicos@druginfo.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	Final
Date of interim/final analysis	14 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 March 2024
Global end of trial reached?	Yes
Global end of trial date	21 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of JM-010 (administered as 2 different dose combinations of JM-010) to that of placebo therapy in reducing dyskinesia severity in PD by evaluating the mean change from Baseline to Week 12 on the Unified Dyskinesia Rating Scale (UDysRS).

Protection of trial subjects:

This study was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki, ICH on GCP Guidelines, applicable International Organization for Standardization ISO 14155 medical device guidelines, and any other applicable national and local legal requirements. The ICF provided to subjects for obtaining subjects' consent was reviewed and approved by the IRB/IEC prior to its use. The investigator or his/her representative explained the study to the subject or his/her legally authorized representative and answered all questions regarding the study. Subjects and/or their legally authorized representative were informed that their participation was voluntary. Subjects or their legally authorized representative were required to sign a statement of informed consent that met the requirements of 21 Code of Federal Regulations 50, local regulations, ICH guidelines, Health Insurance Portability and Accountability Act requirements, where applicable, and the IRB/IEC or study site.

Background therapy:

Subjects were continuing with their usual levodopa treatment regimen for the duration of study participation.

Evidence for comparator:

This was placebo-controlled study.

Actual start date of recruitment	22 July 2019
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	Slovakia: 7
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Korea, Republic of: 35
Worldwide total number of subjects	89
EEA total number of subjects	54

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)	34
From 65 to 84 years	55
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were randomized in a 1:1:1 ratio to receive either 1 of the 2 dose combinations of buspirone and zolmitriptan (JM-010) and 1 placebo, or 2 placebos as per the double-dummy study design.

Pre-assignment

Screening details:

This study comprised of a screening period of 1 to 6 weeks. Subjects with a diagnosis of moderate to severe dyskinesia in Parkinson's disease (PD) completed a screening visit to assess eligibility to participate in the study. The Screening Set included all subjects who signed the inform consent.

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

Blinding implementation details:

This study was double-blinded. This study design included investigator and subject masking.

Arms

Are arms mutually exclusive?	Yes
Arm title	JM-010 0.8/8 mg

Arm description:

Subjects were treated with buspirone 8 mg/zolmitriptan 0.8 mg. The dose strengths of JM-010 were assessed in dosing regimens from 3 to 6 times per day, in order to match the daily doses of L-DOPA administered by each subject.

Arm type	Experimental
Investigational medicinal product name	JM-010 (buspirone 8 mg/zolmitriptan 0.8 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One JM-010 tablet of 8 mg buspirone / 0.8 mg zolmitriptan (166 mg) + 1 placebo tablet (158 mg) were administrated. The time of administration of JM-010 + placebo was dependent on the subject's own levodopa dosing regimen. JM-010 was administrated orally in conjunction with each administration of levodopa during a 12-week double-blind treatment period.

Arm title	JM-010 0.8/4 mg

Arm description:

Subjects were treated with buspirone 4 mg/zolmitriptan 0.8 mg. The dose strengths of JM-010 were assessed in dosing regimens from 3 to 6 times per day, in order to match the daily doses of L-DOPA administered by each subject.

Arm type	Experimental
Investigational medicinal product name	JM-010 (buspirone 4 mg/zolmitriptan 0.8 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One JM-010 tablet of 4 mg buspirone / 0.8 mg zolmitriptan (158 mg) + 1 placebo tablet (166 mg) were administrated. The time of administration of JM-010 + placebo was dependent on the subject's own levodopa dosing regimen. JM-010 was administrated orally in conjunction with each administration of

levodopa during a 12-week double-blind treatment period.

Arm title	Placebo

Arm description:

Subjects were administrated with 1 placebo tablet (158 mg) + 1 placebo tablet (166 mg). The dose strengths of Placebo were assessed in dosing regimens from 3 to 6 times per day, in order to match the daily doses of L-DOPA administered by each subject.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One placebo tablet (158 mg) + 1 placebo tablet (166 mg) were administrated. The time of administration of placebo was dependent on the subject's own levodopa dosing regimen. Placebo was administrated orally in conjunction with each administration of levodopa during a 12-week double-blind treatment period.

Number of subjects in period 1	JM-010 0.8/8 mg	JM-010 0.8/4 mg	Placebo
Started	29	31	29
Completed	20	22	25
Not completed	9	9	4
Serious/Intolerable Adverse Event	2	2	2
Consent withdrawn by subject	2	6	1
Physician decision	2	-	-
Other	1	1	-
Symptoms/Illness Not Consistent with Protocol	2	-	1

Baseline characteristics

Reporting groups	
Reporting group title	JM-010 0.8/8 mg
Reporting group description:	
Subjects were treated with buspirone 8 mg/zolmitriptan 0.8 mg. The dose strengths of JM-010 were assessed in dosing regimens from 3 to 6 times per day, in order to match the daily doses of L-DOPA administered by each subject.	
Reporting group title	JM-010 0.8/4 mg
Reporting group description:	
Subjects were treated with buspirone 4 mg/zolmitriptan 0.8 mg. The dose strengths of JM-010 were assessed in dosing regimens from 3 to 6 times per day, in order to match the daily doses of L-DOPA administered by each subject.	
Reporting group title	Placebo
Reporting group description:	
Subjects were administrated with 1 placebo tablet (158 mg) + 1 placebo tablet (166 mg). The dose strengths of Placebo were assessed in dosing regimens from 3 to 6 times per day, in order to match the daily doses of L-DOPA administered by each subject.	

Reporting group values	JM-010 0.8/8 mg	JM-010 0.8/4 mg	Placebo
Number of subjects	29	31	29
Age categorical Units: Subjects			
Adults (18-64 years)	11	11	12
From 65-84 years	18	20	17
Age continuous Units: years			
median	68.0	68.0	69.0
full range (min-max)	54 to 83	49 to 80	49 to 81
Gender categorical Units: Subjects			
Female	15	18	13
Male	14	13	16

Reporting group values	Total		
Number of subjects	89		
Age categorical Units: Subjects			
Adults (18-64 years)	34		
From 65-84 years	55		
Age continuous Units: years			
median			
full range (min-max)	-		
Gender categorical Units: Subjects			
Female	46		
Male	43		

Subject analysis sets

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS included all randomly assigned subjects who received at least 1 dose of the study treatment, provide baseline assessment and at least 1 post baseline assessment on the UDysRS. The FAS was the primary population for efficacy.

Reporting group values	Full Analysis Set (FAS)		
Number of subjects	85		
Age categorical Units: Subjects			
Adults (18-64 years)	31		
From 65-84 years	54		
Age continuous Units: years median full range (min-max)			
Gender categorical Units: Subjects			
Female	45		
Male	40		

End points

End points reporting groups

Reporting group title	JM-010 0.8/8 mg

Reporting group description:

Subjects were treated with buspirone 8 mg/zolmitriptan 0.8 mg. The dose strengths of JM-010 were assessed in dosing regimens from 3 to 6 times per day, in order to match the daily doses of L-DOPA administered by each subject.

Reporting group title	JM-010 0.8/4 mg

Reporting group description:

Subjects were treated with buspirone 4 mg/zolmitriptan 0.8 mg. The dose strengths of JM-010 were assessed in dosing regimens from 3 to 6 times per day, in order to match the daily doses of L-DOPA administered by each subject.

Reporting group title	Placebo

Reporting group description:

Subjects were administrated with 1 placebo tablet (158 mg) + 1 placebo tablet (166 mg). The dose strengths of Placebo were assessed in dosing regimens from 3 to 6 times per day, in order to match the daily doses of L-DOPA administered by each subject.

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS included all randomly assigned subjects who received at least 1 dose of the study treatment, provide baseline assessment and at least 1 post baseline assessment on the UDysRS. The FAS was the primary population for efficacy.

Primary: UDysRS Total Score from baseline to Week 12 (Full Analysis Set)

End point title	UDysRS Total Score from baseline to Week 12 (Full Analysis Set)

End point description:

Mean Change in the UDysRS Total Score was measured from Baseline to Week 12.

End point type	Primary

End point timeframe:

From Baseline till Week 12

End point values	JM-010 0.8/8 mg	JM-010 0.8/4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	29	28	
Units: UDysRS Total Score				
arithmetic mean (standard deviation)				
Change from Baseline till Week 12	-15.4 (± 12.42)	-10.0 (± 12.05)	-13.9 (± 8.11)	

Statistical analyses

Statistical analysis title	Statistical analysis - JM-010 0.8/8 mg vs Placebo

Statistical analysis description:

Estimates of the mean change and difference in mean change from baseline in the JM-010 treatment arm was compared to the placebo group using a MMRM analysis. The model was: mean change in the

UDysRS total score = treatment arm + visit + baseline + treatment visit. An unstructured covariance matrix was used. If the model failed to converge by using unstructured covariance matrix, compound symmetry matrix was used. Degrees of freedom was calculated using the Kenward-Roger procedure.

Comparison groups	JM-010 0.8/8 mg v Placebo
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.193
Method	Mixed models analysis
Parameter estimate	Least-squared Mean
Point estimate	-4.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.4
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	3.16

Statistical analysis title	Statistical analysis - JM-010 0.8/4 mg vs Placebo

Statistical analysis description:

Estimates of the mean change and difference in mean change from baseline in the JM-010 treatment arm was compared to the placebo group using a MMRM analysis. The model was: mean change in the UDysRS total score = treatment arm + visit + baseline + treatment visit. An unstructured covariance matrix was used. If the model failed to converge by using unstructured covariance matrix, compound symmetry matrix was used. Degrees of freedom was calculated using the Kenward-Roger procedure.

Comparison groups	Placebo v JM-010 0.8/4 mg
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.932
Method	Mixed models analysis
Parameter estimate	Least-squared Mean
Point estimate	-0.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.5
upper limit	5
Variability estimate	Standard error of the mean
Dispersion value	3.13

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During treatment period

Adverse event reporting additional description:

The incidence of all treatment-emergent adverse events (TEAEs) reported during the study was similar between JM-010 0.8/8 mg and placebo groups and higher in the JM-010 0.8/4 mg group. There were no SAEs and deaths reported in Safety Set.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	JM-010 0.8/8 mg

Reporting group description:

Subjects were treated with buspirone 8 mg/zolmitriptan 0.8 mg. The dose strengths of JM-010 were assessed in dosing regimens from 3 to 6 times per day, in order to match the daily doses of L-DOPA administered by each subject.

Reporting group title	JM-010 0.8/4 mg

Reporting group description:

Subjects were treated with buspirone 4 mg/zolmitriptan 0.8 mg. The dose strengths of JM-010 were assessed in dosing regimens from 3 to 6 times per day, in order to match the daily doses of L-DOPA administered by each subject.

Reporting group title	Placebo

Reporting group description:

Subjects were administrated with 1 placebo tablet (158 mg) + 1 placebo tablet (166 mg). The dose strengths of Placebo were assessed in dosing regimens from 3 to 6 times per day, in order to match the daily doses of L-DOPA administered by each subject.

Serious adverse events	JM-010 0.8/8 mg	JM-010 0.8/4 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	0 / 29 (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	JM-010 0.8/8 mg	JM-010 0.8/4 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 29 (20.69%)	5 / 31 (16.13%)	3 / 29 (10.34%)
Nervous system disorders			

On and off phenomenon			
subjects affected / exposed	1 / 29 (3.45%)	4 / 31 (12.90%)	1 / 29 (3.45%)
occurrences (all)	1	4	1
Dizziness			
subjects affected / exposed	2 / 29 (6.90%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	2	0	2
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 29 (10.34%)	1 / 31 (3.23%)	1 / 29 (3.45%)
occurrences (all)	3	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2018	Removed text "patients with moderate to severe dyskinesia" and added "to week 12" in primary objective, added "double-blind, double-dummy" to the study design, updated exclusion criteria, the "pharmacodynamic" assessment was removed from throughout protocol, and added pharmacokinetic endpoints and assessment section.
19 September 2019	Removed text "patients with moderate to severe dyskinesia" from the primary objective in the synopsis; Primary objective updated to include the text "to week 12", added "double-blind, double-dummy" to the study design, updated exclusion criteria.
24 March 2021	Updated number of participating study sites and the total duration of study, Corrected the definition of an overdose and reporting overdose with and without AE/SAE.
15 October 2021	Updated events not meeting the definition of an AE for clarification and activities in Schedule of Events.
25 July 2022	Updated number of study sites and the total duration of study.
06 October 2022	Changed the address of Contera Pharma A/S office to new address.
05 April 2023	Updated eligibility age to 85 years, updated other inclusion and exclusion criteria, updated prior and concomitant therapy, vital signs and schedule of events sections to allow use of selective MAO-B inhibitors, updated method of assigning participants to treatment groups by region of enrollment (Europe and Korea).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported