Clinical trial results:
A Randomized, Placebo-Controlled Phase 2 Study of the Safety, Pharmacokinetics, and Pharmacodynamics of CVT-301 (Levodopa Inhalation Powder) in Patients with Parkinson's Disease and Motor Response Fluctuations ("Off" Episodes)

Summary

EudraCT number	2012-000181-37
Trial protocol	GB
Global end of trial date	29 November 2012

Results information

Result version number	v1 (current)
This version publication date	17 August 2016
First version publication date	17 August 2016

Trial information

Trial identification

Sponsor protocol code	CVT-301-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01617135
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Civitas Therapeutics, Inc., a wholly owned subsidiary of Acorda Therapeutics, Inc.
Sponsor organisation address	420 Saw Mill River Road, Ardsley, United States, 10502
Public contact	Acorda Medical Lead/Scientific Lead, Clinical Development,, Civitas Therapeutics, Inc., a wholly owned subsidiary of Acorda Therapeutics, Inc., +1 914-347-4300,
Scientific contact	Acorda Medical Lead/Scientific Lead, Clinical Development, , Civitas Therapeutics, Inc., a wholly owned subsidiary of Acorda Therapeutics, Inc., +1 914-347-4300,

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	28 June 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 November 2012
Global end of trial reached?	Yes
Global end of trial date	29 November 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterize the safety and tolerability of inhaled CVT 301 in Parkinson’s disease patients experiencing “off” episodes

Protection of trial subjects:

The use of rescue therapy for patients experiencing a prolonged OFF (development of motor fluctuations) period was permitted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 April 2012
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	United Kingdom: 15
Country: Number of subjects enrolled	Serbia: 5
Country: Number of subjects enrolled	Israel: 4
Worldwide total number of subjects	24
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)	12
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The screening period, which took place within 35 days prior to the dosing period, had 2 separate visits. At Screening Visit 1, patients provided written informed consent and were assessed for eligibility in an ON state. At Visit 2, the patient took his/her standard levodopa-containing morning dose along with other prescribed PD medication.

Period 1

Period 1 title	Dosing Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	No
Arm title	Oral CD/LD

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Oral Carbidopa/Levadopa oCD/LD
Investigational medicinal product code	
Other name	SINEMET® Plus
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg/100 mg Tablets

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

2 placebo capsules for 25 mg levadopa fine particle dose (FPD)

Arm title	CVT-301 25mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	CVT-301 (25 mg FPD)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

2 active drug capsules for 25 mg levadopa fine particle dose (FPD)

Arm title	CVT-301 50mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	CVT-301 (50 mg FPD)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

4 active drug capsules for 50 mg levadopa fine particle dose (FPD)

Number of subjects in period 1	Oral CD/LD	Placebo	CVT-301 25mg
Started	24	23	23
Dosing Period (Visit 3 - Visit 6)	24	23	23
Completed	24	23	23

Number of subjects in period 1	CVT-301 50mg
Started	24
Dosing Period (Visit 3 - Visit 6)	24
Completed	24

Baseline characteristics

Reporting groups	
Reporting group title	Dosing Period

Reporting group description: -

Reporting group values	Dosing Period	Total	
Number of subjects	24	24	
Age categorical			
Age categories not defined in Clinical Study Report. See age contnuous characteristics.			
Units: Subjects			
Not Recorded	24	24	
Age continuous			
Units: years			
arithmetic mean	61.3		
standard deviation	± 7.4	-	
Gender categorical			
Units: Subjects			
Female	5	5	
Male	19	19	

End points

End points reporting groups

Reporting group title	Oral CD/LD
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	CVT-301 25mg
Reporting group description: -	
Reporting group title	CVT-301 50mg
Reporting group description: -	

Primary: Pharmacokinetics Cmax

End point title	Pharmacokinetics Cmax[1]

End point description:

Variable baseline-adjusted plasma concentration-time profiles for the following;
- maximum plasma concentration (Cmax)

End point type	Primary

End point timeframe:

0-30 minutes post-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: Results of the trial are considered valid.

End point values	Oral CD/LD	Placebo	CVT-301 25mg	CVT-301 50mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	23	23	24
Units: ng/mL				
arithmetic mean (standard deviation)				
Cmax 0-10	242 (± 379)	45 (± 85)	273 (± 183)	578 (± 315)
Cmax 0-30	620 (± 810)	49 (± 87)	322 (± 201)	690 (± 351)

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetics AUC

End point title	Pharmacokinetics AUC[2]

End point description:

Variable baseline adjusted plasma concentration-time profiles for the below:
- area under the concentration time curve (AUC)

End point type	Primary

End point timeframe:

0-30 minutes 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: Results of the trial are considered valid.

End point values	Oral CD/LD	Placebo	CVT-301 25mg	CVT-301 50mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	23	23	24
Units: ng-min/mL				
arithmetic mean (standard deviation)				
AUC 0-10	758 (± 1166)	285 (± 580)	1957 (± 1522)	3833 (± 2202)
AUC 0-30	9813 (± 14701)	1015 (± 2202)	7188 (± 4739)	15711 (± 8296)

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetics Tmax

End point title	Pharmacokinetics Tmax[3]

End point description:

Variable baseline-adjusted plasma concentration-time profiles for the following;
- time to reach Cmax (T Cmax)
- time to maximum concentration (Tmax)

End point type	Primary

End point timeframe:

up to 80 minutes 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: Results of the trial are considered valid.

End point values	Oral CD/LD	Placebo	CVT-301 25mg	CVT-301 50mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	23	23	24
Units: min				
arithmetic mean (standard deviation)				
T Cmax 50	51.6 (± 33.2)	13.4 (± 26.5)	4.5 (± 2.34)	4.96 (± 2.43)
Tmax	78 (± 40)	55 (± 57)	16 (± 10)	23 (± 24)

Statistical analyses

No statistical analyses for this end point

Primary: UPDRS III motor score

End point title	UPDRS III motor score[4]

End point description:

The Unified Parkinson's Disease Rating Scale, Part III motor section (UPDRS III) is the motor section of the UPDRS examination, given by interview with actions performed by the patient. Some questions required multiple ratings to be assigned to each extremity. The areas addressed by this exam included speech, facial expression, tremor at rest, postural tremor, rigidity, finger taps, hand movements, rapid alternating movement (hands), leg agility, arising from a chair, posture, gait, postural stability, and body bradykinesia/hypokinesia.

Early effect, defined as average response of assessments at 0-30 minutes after the dose of study medication.

End point type	Primary

End point timeframe:

pre-dose and up to 180 minutes 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: Results of the trial are considered valid.

End point values	Oral CD/LD	Placebo	CVT-301 25mg	CVT-301 50mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24[5]	22[6]	23	24
Units: number/score on a scale				
arithmetic mean (standard deviation)				
Average response	-13.3 (± 5.42)	-3.2 (± 5.71)	-5.2 (± 5.89)	-7.5 (± 6.64)
Best response	-23.3 (± 6.46)	-10.8 (± 7.91)	-12.3 (± 8.55)	-16.2 (± 7.85)
Early effect AUC 0-30	1854.04 (± 743.56)	1905.33 (± 946.66)	1908.8 (± 634.37)	1795.42 (± 750.83)

Notes:

[5] - Early effect AUC 0-30: Number of subjects 23

[6] - Early effect AUC 0-30: Number of subjects 23

Statistical analyses

No statistical analyses for this end point

Primary: Tapping Test

End point title	Tapping Test[7]

End point description:

The finger tapping test requires a patient to alternately tap 2 manual counters that are separated by 20 cm for 30 seconds using one hand, and the number of taps per time interval is recorded.

End point type	Primary

End point timeframe:

up to 180 minutes 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: Results of the trial are considered valid.

End point values	Oral CD/LD	Placebo	CVT-301 25mg	CVT-301 50mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	23	23	24
Units: number of taps				
arithmetic mean (standard deviation)				
Average response	7.9 (± 7.92)	1.5 (± 7.36)	4.4 (± 9.74)	6.5 (± 8.51)
Best response	19.2 (± 11.76)	8.3 (± 9.81)	13.5 (± 12.12)	16 (± 12)

Early effect AUC 0-30	1778.6 (± 651.31)	1827.7 (± 529.55)	1983.9 (± 667.5)	1954.6 (± 637.69)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 12 weeks

Adverse event reporting additional description:

Events were classified as treatment-emergent if they started on or after the first dose of study drug administration at Visit 3 (start of 2-6 week dosing period) and up to and including the completion/termination date.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15

Reporting groups

Reporting group title	Oral CD/LD
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	CVT-301 25mg
Reporting group description: -	
Reporting group title	CVT-301 50mg
Reporting group description: -	

Serious adverse events	Oral CD/LD	Placebo	CVT-301 25mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 23 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	CVT-301 50mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Oral CD/LD	Placebo	CVT-301 25mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 24 (8.33%)	1 / 23 (4.35%)	5 / 23 (21.74%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Parkinson's disease			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	5 / 23 (21.74%)
occurrences (all)	0	0	10
Rhinorrhoea			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	CVT-301 50mg		
Total subjects affected by non-serious adverse events			

subjects affected / exposed	8 / 24 (33.33%)		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Parkinson's disease			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 24 (20.83%)		
occurrences (all)	10		
Rhinorrhoea			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	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