



Clinical trial results:

A Phase 2b, Randomized, Double-blind, Placebo-controlled Study Investigating the Efficacy and Safety of Inhaled CVT-301 (Levodopa Inhalation Powder) in Parkinson's Disease Patients With Motor Response Fluctuations (OFF Phenomena).

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2012-005822-31 |
| Trial protocol | GB IT |
| Global end of trial date | 21 January 2014 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 06 June 2016 |
| First version publication date | 14 August 2015 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | CVT-301-003 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|--------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01777555 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Sample data: Sample data |

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 & Medical Affairs (CDMA), +1 914-347-4300, |
| Scientific contact | Acorda Medical Lead/Scientific Lead, CDMA, +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 | 18 July 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 21 January 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial is to compare the effects of CVT-301 Dose Level 2 (DL2; high dose) and placebo on the mean change from pre-dose in average UPDRS Part 3 motor score at 10 to 60 minutes following treatment of patients experiencing an OFF episode at the end-of-treatment (EOT) visit (Visit 6).

Protection of trial subjects:

n/a

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 15 April 2013 |
| 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 | Italy: 10 |
| Country: Number of subjects enrolled | United Kingdom: 4 |
| Country: Number of subjects enrolled | United States: 64 |
| Country: Number of subjects enrolled | Serbia: 8 |
| Worldwide total number of subjects | 86 |
| EEA total number of subjects | 14 |

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) | 49 |
| From 65 to 84 years | 37 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

| | |
|------------------------------|-------------------|
| Number of subjects started | 89 ^[1] |
| Number of subjects completed | 86 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|---|
| Reason: Number of subjects | Withdrawn from study before receiving study drug: 3 |
|----------------------------|---|

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The number of patients (89) were randomized. (3) patients were withdrawn from study before receiving any study drug. (86) patients continued to Treatment Period 1.

Period 1

| | |
|------------------------------|--|
| Period 1 title | Treatment Period |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Assessor |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description: -

| | |
|--|----------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Inhalation use |

Dosage and administration details:

Placebo powder was intended to provide a sensation of dose administration, but was not intended to provide a respirable dose.

| | |
|------------------|---------|
| Arm title | CVT-301 |
|------------------|---------|

Arm description: -

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | CVT-301 |
| Investigational medicinal product code | |
| Other name | Levodopa |
| Pharmaceutical forms | Inhalation powder, hard capsule |
| Routes of administration | Inhalation use |

Dosage and administration details:

CVT-301 capsule designed to deliver an approximate respirable dose.

| Number of subjects in period 1 | Placebo | CVT-301 |
|--------------------------------|---------|---------|
| Started | 43 | 43 |
| Completed | 43 | 43 |

Period 2

| | |
|------------------------------|--|
| Period 2 title | Follow-up Period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Assessor |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description: -

| | |
|--|----------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Inhalation use |

Dosage and administration details:

Placebo consists of inhalation grade lactose monohydrate 120MS, United States Pharmacopeia (USP).

| | |
|------------------|---------|
| Arm title | CVT-301 |
|------------------|---------|

Arm description: -

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | CVT-301 |
| Investigational medicinal product code | |
| Other name | Levodopa |
| Pharmaceutical forms | Inhalation powder, hard capsule |
| Routes of administration | Inhalation use |

Dosage and administration details:

CVT-301 capsule designed to deliver an approximate respirable dose.

| Number of subjects in period 2 | Placebo | CVT-301 |
|--------------------------------|---------|---------|
| Started | 43 | 43 |
| Completed | 36 | 39 |
| Not completed | 7 | 4 |
| Consent withdrawn by subject | 3 | 3 |

| | | |
|--------------------------|---|---|
| Adverse event, non-fatal | 3 | 1 |
| Lost to follow-up | 1 | - |

Baseline characteristics

Reporting groups

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

| |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

| | |
|-----------------------|---------|
| Reporting group title | CVT-301 |
|-----------------------|---------|

| |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

| Reporting group values | Placebo | CVT-301 | Total |
|---|----------------|--------------|-------|
| Number of subjects | 43 | 43 | 86 |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 62.7 ± 9.08 | 62 ± 8.36 | - |
| Gender categorical Units: Subjects | | | |
| Female | 11 | 18 | 29 |
| Male | 32 | 25 | 57 |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | CVT-301 |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | CVT-301 |
| Reporting group description: - | |
| Subject analysis set title | ITT Population |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: The Intent-to-Treat (ITT) population will include all patients who received at least one dose of inhaled CVT-301 or placebo. Patients will be analyzed according to randomized treatment. The ITT Population will be used for all analyses of efficacy endpoints and summaries of patient demographic and baseline characteristics. | |
| Subject analysis set title | Safety Population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The Safety Population will include all patients who received at least one dose of inhaled CVT-301 or placebo. Patients will be analyzed according to treatment received. The Safety Population will be used for all analyses of safety endpoints. | |

Primary: UPDRS Part 3 Score Mean Change From Predose to 10 to 60 Minutes Postdose at Visit 6

| | |
|--|---|
| End point title | UPDRS Part 3 Score Mean Change From Predose to 10 to 60 Minutes Postdose at Visit 6 |
| End point description: | |
| End point type | Primary |
| End point timeframe: Predose to 10 to 60 Minutes Postdose | |

| End point values | Placebo | CVT-301 | | |
|-------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 42 | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | -3.07 (\pm 1.54) | -10.02 (\pm 1.5) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | UPDRS Part 3 Score Mean Change at Visit 6 |
| Statistical analysis description: MMRM model uses UPDRS Part III total score at 10 to 60 minutes at visits 4, 5, and 6 as the dependent variable, and includes baseline PD severity, country, treatment, visit, and treatment-by-visit interaction | |

as factors and baseline UPDRS Part III score, screening score in OFF state, as a covariate.

| | |
|---|----------------------------|
| Comparison groups | Placebo v CVT-301 |
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| P-value | < 0.001 ^[2] |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -6.95 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.31 |
| upper limit | -3.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.5 |

Notes:

[1] - Mixed effect Model Repeat Measurement

[2] - CVT-301 p-value at Visit 6

Dispersion value SE of the mean shown below is for CVT-301. Placebo (SE) dispersion value is 1.544

Secondary: Change from pre-dose in the average UPDRS Part 3 motor score at the end of 1 week of treatment (Visit 4)

| | |
|----------------------------|--|
| End point title | Change from pre-dose in the average UPDRS Part 3 motor score at the end of 1 week of treatment (Visit 4) |
| End point description: | |
| ITT Population | |
| End point type | Secondary |
| End point timeframe: | |
| 10 to 60 minutes post-dose | |

| End point values | Placebo | CVT-301 | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 42 | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | -5.3 (± 1.53) | -9.9 (± 1.49) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients achieving objective UPDRS 3 motor response (≥30%)

| | |
|--|--|
| End point title | Number of patients achieving objective UPDRS 3 motor response (≥30%) |
| End point description: | |
| ITT Population | |
| Objective motor response is defined as a patient having ≥30% reduction in the UPDRS Part 3 total score | |

from pre-dose to post-dose at any time point post-dose.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From 10 to 60 minutes post-dose visits 4, 5 and 6. | |

| End point values | Placebo | CVT-301 | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Number | | | | |
| Visit 4 (N=40/42) $\geq 30\%$ reduction | 15 | 27 | | |
| Visit 5 (N=39/40) $\geq 30\%$ reduction | 11 | 28 | | |
| Visit 6 (N=36/38) $\geq 30\%$ reduction | 10 | 27 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change and percent change in UPDRS Part 3 Total Score at specified time points from Pre-dose to Post-dose

| | |
|-----------------|---|
| End point title | Change and percent change in UPDRS Part 3 Total Score at specified time points from Pre-dose to Post-dose |
|-----------------|---|

End point description:

| | |
|---------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 10 to 60 minutes following treatment. | |

| End point values | Placebo | CVT-301 | | |
|---|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Percent change/Score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 4 Change 10 min post-dose (N=40/42) | -3.2 (\pm 6.59) | -6.1 (\pm 7.96) | | |
| Visit 4 Percent Change 10 min post-dose (N=40/42) | -9.74 (\pm 17.86) | -15.18 (\pm 30.27) | | |
| Visit 4 Change 20 min post-dose (N=40/42) | -5.9 (\pm 7.83) | -10 (\pm 9.32) | | |
| Visit 4 Percent Change 20 min post-dose (N=40/42) | -18.25 (\pm 22) | -27.79 (\pm 33.95) | | |
| Visit 4 Change 30 min post-dose (N=40/42) | -6.1 (\pm 7.71) | -11 (\pm 9.2) | | |
| Visit 4 Percent Change 30 min post-dose (N=40/42) | -19.25 (\pm 25.14) | -31.83 (\pm 28.45) | | |
| Visit 4 Change 60 min post-dose (N=40/42) | -4.2 (\pm 6.51) | -9.3 (\pm 11.12) | | |

| | | | | |
|---|------------------|------------------|--|--|
| Visit 4 Percent Change 60 min post-dose (N=40/42) | -13.73 (± 23.49) | -24.22 (± 40.68) | | |
| Visit 5 Change 10 min Post-dose (N=38/40) | -2.5 (± 7.81) | -4.6 (± 7.11) | | |
| Visit 5 Percent Change 10 min Post-dose (N=38/40) | -3.72 (± 25.02) | -13.96 (± 20.87) | | |
| Visit 5 Change 20 min Post-dose (N=39/40) | -4.5 (± 7.53) | -9.8 (± 9.06) | | |
| Visit 5 Percent Change 20 min Post-dose (N=39/40) | -9.71 (± 27.56) | -28.66 (± 25.7) | | |
| Visit 5 Change 30 min Post-dose (N=39/40) | -3.4 (± 8.27) | -11.7 (± 10.8) | | |
| Visit 5 Percent Change 30 min Post-dose (N=39/40) | -5.66 (± 30.63) | -33.55 (± 26.47) | | |
| Visit 5 Change 60 min Post-dose (N=39/40) | -1.9 (± 6.07) | -11.4 (± 11.98) | | |
| Visit 5 Percent Change 60 min Post-dose (N=39/40) | -0.91 (± 31.86) | -33.02 (± 30.53) | | |
| Visit 6 Change 10 min Post-dose (N=36/38) | -2 (± 7.48) | -4.9 (± 7.82) | | |
| Visit 6 Percent Change 10 min Post-dose (N=36/38) | -3.46 (± 27.49) | -14.45 (± 20) | | |
| Visit 6 Change 20 min Post-dose (N=36/38) | -3.8 (± 8.96) | -8.9 (± 9.78) | | |
| Visit 6 Percent Change 20 min Post-dose (N=36/38) | -8.81 (± 28.54) | -27.73 (± 27.42) | | |
| Visit 6 Change 30 min Post-dose (N=36/38) | -3.3 (± 7.56) | -11.6 (± 9.67) | | |
| Visit 6 Percent Change 30 min Post-dose (N=36/38) | -7.66 (± 27.35) | -35.27 (± 27.56) | | |
| Visit 6 Change 60 min Post-dose (N=36/38) | -1.6 (± 6.53) | -11.2 (± 9.83) | | |
| Visit 6 Percent Change 60 min Post-dose (N=36/38) | -2.47 (± 25.88) | -33.82 (± 28.22) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Examiner-rated Time to Resolution of OFF Episodes to ON State

| | |
|-----------------|---|
| End point title | Examiner-rated Time to Resolution of OFF Episodes to ON State |
|-----------------|---|

End point description:

Time to Resolution of OFF Episodes to ON State is calculated as (Time patient turns "ON" – Time of study drug administration). Measure type number = 25% Quantile
999 number = NE (not equatable)

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Following observed treatment of patients experiencing an Off episode at each visit

| End point values | Placebo | CVT-301 | | |
|----------------------------------|------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Minutes | | | | |
| number (confidence interval 95%) | | | | |
| Visit 4 (N=40/42) | 22.5 (13 to 30) | 16 (9 to 20) | | |
| Visit 5 (N=39/39) | 17 (8 to 38) | 15 (9 to 20) | | |
| Visit 6 (N=36/37) | 13.5 (10 to 999) | 10 (8 to 18) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time from Dosing to Dyskinesia Onset

| | |
|--|--------------------------------------|
| End point title | Time from Dosing to Dyskinesia Onset |
| End point description: | |
| ITT Population | |
| End point type | Secondary |
| End point timeframe: | |
| Following study medication administration at each visit. | |

| End point values | Placebo | CVT-301 | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Minutes | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 4 (N=4/5) | 21 (± 9.9) | 44.8 (± 16.98) | | |
| Visit 5 (N=2/12) | 14 (± 12.73) | 43 (± 27.76) | | |
| Visit 6 (N=2/10) | 29 (± 33.94) | 29.3 (± 11.17) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence and Severity of Dyskinesia Visit 4

| | |
|---|---|
| End point title | Occurrence and Severity of Dyskinesia Visit 4 |
| End point description: | |
| Dyskinesia in Parkinson's Disease (DPD) | |
| End point type | Secondary |
| End point timeframe: | |
| Following study medication at visit 4 (Week 2). | |

| End point values | Placebo | CVT-301 | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Number | | | | |
| DPD Turned ON Post Inhaled Treatment | 18 | 28 | | |
| DPD Among Patients Turned ON Post Treatment- Yes | 4 | 5 | | |
| DPD Among Patients Turned ON Post Treatment- No | 14 | 23 | | |
| Dyskinesia Among All Patients - Yes | 4 | 5 | | |
| Dyskinesia Among All Patients - No | 36 | 37 | | |
| Severity of Dyskinesia - Mild | 1 | 4 | | |
| Severity of Dyskinesia - Moderate | 2 | 1 | | |
| Severity of Dyskinesia - Severe | 0 | 0 | | |
| Severity of Dyskinesia - Unknown | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence and Severity of Dyskinesia Visit 5

| | |
|------------------------|---|
| End point title | Occurrence and Severity of Dyskinesia Visit 5 |
| End point description: | Dyskinesia in Parkinson's Disease (DPD) |
| End point type | Secondary |
| End point timeframe: | Following study medication at visit 5 (Week 3). |

| End point values | Placebo | CVT-301 | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Number | | | | |
| Turned ON Post Inhaled Treatment | 16 | 30 | | |
| DPD Among Patients Turned ON Post Treatment- Yes | 1 | 12 | | |
| DPD Among Patients Turned ON Post Treatment- No | 15 | 18 | | |
| Dyskinesia Among All Patients - Yes | 2 | 12 | | |
| Dyskinesia Among All Patients - No | 37 | 28 | | |
| Severity of Dyskinesia - Mild | 1 | 12 | | |
| Severity of Dyskinesia - Moderate | 1 | 0 | | |
| Severity of Dyskinesia - Severe | 0 | 0 | | |
| Severity of Dyskinesia - Unknown | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence and Severity of Dyskinesia Visit 6

| | |
|-----------------|---|
| End point title | Occurrence and Severity of Dyskinesia Visit 6 |
|-----------------|---|

End point description:

Dyskinesia in Parkinson's Disease (DPD)

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Following study medication at visit 6 (Week 5).

| End point values | Placebo | CVT-301 | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Number | | | | |
| Turned ON Post Inhaled Treatment | 13 | 30 | | |
| DPD Among Patients Turned ON Post Treatment- Yes | 2 | 12 | | |
| DPD Among Patients Turned ON Post Treatment- No | 11 | 18 | | |
| Dyskinesia Among All Patients - Yes | 2 | 12 | | |
| Dyskinesia Among All Patients - No | 34 | 26 | | |
| Severity of Dyskinesia - Mild | 2 | 9 | | |
| Severity of Dyskinesia - Moderate | 0 | 2 | | |
| Severity of Dyskinesia - Severe | 0 | 0 | | |
| Severity of Dyskinesia - Unknown | 0 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients achieving objective UPDRS III motor response ($\geq 20\%$ reduction, ≥ 6 point and ≥ 11 point reduction)

| | |
|-----------------|--|
| End point title | Number of patients achieving objective UPDRS III motor response ($\geq 20\%$ reduction, ≥ 6 point and ≥ 11 point reduction) |
|-----------------|--|

End point description:

ITT Population

Objective motor response is defined as a patient having $\geq 20\%$ reduction, ≥ 6 point and ≥ 11 point reduction in the UPDRS Part III total score from pre-dose to post-dose at any time point post-dose.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From 10 to 60 minutes post-dose visits 4, 5 and 6. | |

| End point values | Placebo | CVT-301 | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Number | | | | |
| Visit 4 (N=40/42) ≥20% reduction | 21 | 31 | | |
| Visit 5 (N=39/40) ≥20% reduction | 14 | 31 | | |
| Visit 6 (N=36/38) ≥20% reduction | 13 | 31 | | |
| Visit 4 (N=40/42) ≥6 point reduction | 22 | 32 | | |
| Visit 5 (N=39/40) ≥6 point reduction | 17 | 32 | | |
| Visit 6 (N=36/38) ≥6 point reduction | 13 | 31 | | |
| Visit 4 (N=40/42) ≥11 point reduction | 11 | 24 | | |
| Visit 5 (N=39/40) ≥11 point reduction | 11 | 26 | | |
| Visit 6 (N=36/38) ≥11 point reduction | 10 | 25 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean time from study treatment to resolution of an OFF episode to an ON state during 2 week at-home period

| | |
|------------------------------|--|
| End point title | Mean time from study treatment to resolution of an OFF episode to an ON state during 2 week at-home period |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| At-home treatment weeks 1-2. | |

| End point values | Placebo | CVT-301 | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Minutes | | | | |
| least squares mean (standard error) | 59.3 (± 6.92) | 48.9 (± 6.78) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean daily ON time without dyskinesia, ON time with dyskinesia (troublesome and non-troublesome), and OFF time from PD diaries

| | |
|-----------------|--|
| End point title | Mean daily ON time without dyskinesia, ON time with dyskinesia (troublesome and non-troublesome), and OFF time from PD diaries |
|-----------------|--|

End point description:

ITT Population

ON time with dyskinesia (troublesome and non-troublesome)

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Screening period and Treatment Weeks 1, 2 and 4.

| End point values | Placebo | CVT-301 | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Hours | | | | |
| least squares mean (standard error) | | | | |
| Week 1 ON time without dyskinesia | 0.05 (± 0.42) | 0.43 (± 0.42) | | |
| Week 2 ON time without dyskinesia | 0.38 (± 0.46) | 0.7 (± 0.46) | | |
| Week 4 ON time without dyskinesia | 0.19 (± 0.48) | 0.59 (± 0.47) | | |
| Week 1 ON time with dyskinesia | 0.54 (± 0.26) | 0.3 (± 0.25) | | |
| Week 2 ON time with dyskinesia | 0.35 (± 0.22) | 0.17 (± 0.22) | | |
| Week 4 ON time with dyskinesia | 0.4 (± 0.27) | 0.7 (± 0.27) | | |
| Week 1 OFF time | -0.72 (± 0.35) | -0.99 (± 0.35) | | |
| Week 2 OFF time | -0.77 (± 0.37) | -1.06 (± 0.37) | | |
| Week 4 OFF time | -0.77 (± 0.38) | -1.64 (± 0.37) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treated OFF episodes that resolve to an ON state at pre-specified time intervals (minutes) after study treatment

| | |
|-----------------|--|
| End point title | Number of treated OFF episodes that resolve to an ON state at pre-specified time intervals (minutes) after study treatment |
|-----------------|--|

End point description:

Cumulative number indicates the total number of resolved episodes during the week in question.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Treatment Weeks 1, 2, 3 and 4

| End point values | Placebo | CVT-301 | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Cumulative Number | | | | |
| Week 1 (≤ 5 min) | 10 | 41 | | |
| Week 1 (≤ 10 min) | 53 | 75 | | |
| Week 1 (≤ 20 min) | 176 | 195 | | |
| Week 1 (≤ 30 min) | 258 | 271 | | |
| Week 1 (≤ 45 min) | 323 | 338 | | |
| Week 1 (≤ 180 min) | 495 | 497 | | |
| Week 2 (≤ 5 min) | 20 | 23 | | |
| Week 2 (≤ 10 min) | 35 | 72 | | |
| Week 2 (≤ 20 min) | 145 | 170 | | |
| Week 2 (≤ 30 min) | 215 | 238 | | |
| Week 2 (≤ 45 min) | 274 | 307 | | |
| Week 2 (≤ 180 min) | 474 | 444 | | |
| Week 3 (≤ 5 min) | 23 | 15 | | |
| Week 3 (≤ 10 min) | 70 | 52 | | |
| Week 3 (≤ 20 min) | 168 | 170 | | |
| Week 3 (≤ 30 min) | 240 | 232 | | |
| Week 3 (≤ 45 min) | 354 | 302 | | |
| Week 3 (≤ 180 min) | 499 | 428 | | |
| Week 4 (≤ 5 min) | 29 | 21 | | |
| Week 4 (≤ 10 min) | 78 | 62 | | |
| Week 4 (≤ 20 min) | 129 | 170 | | |
| Week 4 (≤ 30 min) | 188 | 253 | | |
| Week 4 (≤ 45 min) | 256 | 316 | | |
| Week 4 (≤ 180 min) | 456 | 440 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 10 weeks.

Adverse event reporting additional description:

Treatment Emergent Adverse Events (TEAEs)

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 15.1 |
|--------------------|------|

Reporting groups

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

Reporting group description: -

| | |
|-----------------------|---------|
| Reporting group title | CVT-301 |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events | Placebo | CVT-301 | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 43 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Nervous system disorders | | | |
| Drop attacks | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 4 %

| Non-serious adverse events | Placebo | CVT-301 | |
|---|-----------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 6 / 43 (13.95%) | 17 / 43 (39.53%) | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | 3 / 43 (6.98%) | |
| occurrences (all) | 4 | 3 | |
| Headache | | | |

| | | | |
|---|--|--|--|
| subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 3 | 2 / 43 (4.65%) 2 | |
| General disorders and administration site conditions Oedema peripheral subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | 2 / 43 (4.65%) 2 | |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 3 / 43 (6.98%) 4 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Sputum discoloured subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 0 / 43 (0.00%) 0 | 3 / 43 (6.98%) 4 2 / 43 (4.65%) 3 | |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 2 / 43 (4.65%) 2 | |

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