Clinical trial results:
An Open-Label, Long-Term Safety, Tolerability, and Efficacy Study of TEV-50717 (Deutetrabenazine) for the Treatment of Dyskinesia in Cerebral Palsy in Children and Adolescents (Open RECLAIM-DCP)

Summary

EudraCT number	2019-001807-19
Trial protocol	ES PL DK IT
Global end of trial date	14 February 2023

Results information

Result version number	v1 (current)
This version publication date	30 August 2023
First version publication date	30 August 2023

Trial information

Trial identification

Sponsor protocol code	TV50717-CNS-30081

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04200352
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Teva Branded Pharmaceutical Products R&D, Inc.
Sponsor organisation address	145 Brandywine Parkway, West Chester, United States, 19380
Public contact	Director, Clinical Research, Teva Branded Pharmaceutical Products, R&D Inc., MedInfo@tevaeu.com
Scientific contact	Director, Clinical Research, Teva Branded Pharmaceutical Products, R&D Inc., MedInfo@tevaeu.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 February 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 February 2023
Global end of trial reached?	Yes
Global end of trial date	14 February 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the safety and tolerability of long-term therapy with TEV-50717 in children and adolescents with dyskinesia in cerebral palsy (DCP).

Protection of trial subjects:

This study was conducted in full accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Consolidated Guideline (E6) and any applicable national and local laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 February 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 5
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Russian Federation: 7
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Ukraine: 14
Country: Number of subjects enrolled	Israel: 2
Worldwide total number of subjects	44
EEA total number of subjects	13

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)	25
Adolescents (12-17 years)	17
Adults (18-64 years)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 44 participants with DCP from Study TV50717-CNS-30080 (NCT03813238) rolled over into Study TV50717-CNS-30081.

Period 1

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

Arms

Arm title	TEV-50717

Arm description:

TEV-50717 was administered as oral tablets once daily for up to 53 weeks (7 weeks dose titration and 46 weeks maintenance). From Week 1 through Week 7, the dose of TEV-50717 was adjusted according to the titrations scheme (based on body weight and cytochrome P450 2D6 [CYP2D6] impairment status at baseline) to identify a dose level that optimally reduced dyskinesia (as determined by the investigator, as indicated by a reduction in the clinical global impression of improvement [CGI-I]) and was well tolerated. After titration, participants continued to receive their maintenance dose over the next 46 weeks.

Arm type	Experimental
Investigational medicinal product name	TEV-50717
Investigational medicinal product code	SD-809
Other name	Deutetrabenazine
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

TEV-50717 was administered per dose and schedule specified in the arm description.

Number of subjects in period 1	TEV-50717
Started	44
Received at least 1 dose of study drug	44
Completed	24
Not completed	20
Adverse event, serious fatal	1
Adverse event, non-fatal	6
Other than specified	6
Withdrawal by parent/guardian	6
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	TEV-50717

Reporting group description:

TEV-50717 was administered as oral tablets once daily for up to 53 weeks (7 weeks dose titration and 46 weeks maintenance). From Week 1 through Week 7, the dose of TEV-50717 was adjusted according to the titrations scheme (based on body weight and cytochrome P450 2D6 [CYP2D6] impairment status at baseline) to identify a dose level that optimally reduced dyskinesia (as determined by the investigator, as indicated by a reduction in the clinical global impression of improvement [CGI-I]) and was well tolerated. After titration, participants continued to receive their maintenance dose over the next 46 weeks.

Reporting group values	TEV-50717	Total	
Number of subjects	44	44	
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	11.1		
standard deviation	± 3.56	-	
Sex: Female, Male Units: participants			
Female	15	15	
Male	29	29	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	42	42	
More than one race	0	0	
Unknown or Not Reported	2	2	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	2	
Not Hispanic or Latino	39	39	
Unknown or Not Reported	3	3	
Extrapyramidal Symptom Rating Scale (ESRS) Subscale I Total Score			
ESRS subscale I is a 7-item subjective questionnaire to evaluate parkinsonism, akathisia, dystonia, and dyskinesia. ESRS I is scored on a 4-point scale (0=absent, 1=Mild, 2=Moderate, 3=Severe) for each item. The evaluation takes into account the verbal report of the participant on 1) frequency and duration of symptoms during the day, 2) number of days the symptom was present during the last week, and 3) subjective evaluation of intensity of symptom by the participant. Total score was the sum of 7 items ranging from 0 (absent) to 28 (severe). Higher scores indicate greater severity of disorder.			
Units: units on a scale			
arithmetic mean	9.7		
standard deviation	± 3.94	-	

ESRS Subscale II Total Score			
The ESRS subscale II is a 17-item questionnaire to evaluate parkinsonism and akathisia. The ESRS II consists of the following parts: tremor (0 [none]–48 [severe]), gait and posture (0 [none]–6 [severe]), postural stability (0 [none]-6 [severe]), rigidity (0 [none]–24 [severe]), expressive automatic movements (0 [none]–6 [severe]), bradykinesia (0 [none]-6 [severe]), and akathisia (0 [none]–6 [severe]). Total score was the sum of the 17 items ranging from 0 (absent) to 102 (severe). Higher scores indicate greater severity of disorder.			
Units: units on a scale arithmetic mean standard deviation	 20.7 ± 19.73	 -	
Epworth Sleepiness Scale (ESS) Total Score			
ESS is a self-administered questionnaire composed of 8 questions that provide a measure of a participant's general level of daytime sleepiness. Responders were asked to rate their chances of falling asleep while engaged at 8 different activities, on a 4-point scale: 0 = would never fall asleep; 1=slight chance of falling asleep; 2=moderate chance of falling asleep; 3=high chance of falling asleep. Total score was calculated as the sum of 8 item scores ranging from 0 (never) to 24 (high chance of falling asleep). Higher scores indicate high chances of falling asleep.			
Units: units on a scale arithmetic mean standard deviation	 2.0 ± 2.79	 -	
CBCL Syndrome Total Score			
CBCL Syndrome Scale comprises 113 questions related to problem behaviors. For each item, responses are recorded on a scale: 0 = Not True; 1 = Somewhat or Sometimes True; 2 = Very True or Often True. Problem behaviors are scored on the following 8 empirically based syndromes: anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behavior, and aggressive behavior. CBCL syndrome total score ranged from 0 (no problem) to 226 (lesser problem). Higher scores indicate greater problems in child behavior.			
Units: units on a scale arithmetic mean standard deviation	 30.7 ± 21.06	 -	
Child Behavior Checklist (CBCL) Competence Total Score			
CBCL Competence Scale (Parts I to VII) assesses various activities (sports, hobbies, games, organizations, clubs, teams, groups, jobs, and chores), interpersonal relationships, and academic performance. Checklists having 120 questions consist of a number of statements about child's behavior and responses which are recorded on a scale: 0 = Not True; 1 = Somewhat True; 2 = Very True or Often True. CBCL competence total score ranged from 0 (no problem) to 240 (lesser problem). Higher scores indicate greater problems in child behavior. Participants evaluable for this Baseline measure = 33.			
Units: units on a scale arithmetic mean standard deviation	 11.70 ± 4.392	 -	

End points

End points reporting groups

Reporting group title	TEV-50717

Reporting group description:

TEV-50717 was administered as oral tablets once daily for up to 53 weeks (7 weeks dose titration and 46 weeks maintenance). From Week 1 through Week 7, the dose of TEV-50717 was adjusted according to the titrations scheme (based on body weight and cytochrome P450 2D6 [CYP2D6] impairment status at baseline) to identify a dose level that optimally reduced dyskinesia (as determined by the investigator, as indicated by a reduction in the clinical global impression of improvement [CGI-I]) and was well tolerated. After titration, participants continued to receive their maintenance dose over the next 46 weeks.

Primary: Number of Participants (Aged ≥12 Years) With Columbia-Suicide Severity Rating Scale (C-SSRS) Outcomes (Worst Overall Finding)

End point title	Number of Participants (Aged ≥12 Years) With Columbia-Suicide Severity Rating Scale (C-SSRS) Outcomes (Worst Overall Finding)[1]

End point description:

Participants were placed into categories for suicidal ideation or behavior and non-suicidal self-injurious behavior based on their responses to various questions. For suicidal ideation or behavior, following categories were used: None; Wish to be dead; Non-specific active suicidal thoughts; Any methods (not plan) without intent to act; Some intent to act, without specific plan; Specific plan and intent; Preparatory acts or behavior; Aborted attempt; Interrupted attempt; Actual attempt; and Suicide. For non-suicidal self-injurious behavior, "No or yes" categories were used. Number of participants with worst overall finding of suicidal ideation or suicidal behavior and non-suicidal self-injurious behavior from Baseline to Week 54 are reported. ITT analysis set= all enrolled participants, regardless of whether or not a participant took any TEV-50717. 'Overall number of participants analyzed' = participants who had a baseline value and at least 1 post-baseline value for this endpoint.

End point type	Primary

End point timeframe:

Baseline to Week 54

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: No statistical analyses were planned for this endpoint.

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: participants				
Suicidal ideation/behavior - None	18			
Suicidal ideation/behavior - Wish to be dead	0			
Non-specific active suicidal thoughts	0			
Any method (not plan) without intent to act	0			
Some intent to act, without specific plan	0			
Specific plan and intent	0			
Preparatory acts or behavior	0			
Suicidal ideation/behavior - Aborted attempt	0			
Suicidal ideation/behavior - Interrupted attempt	0			

Suicidal ideation/behavior - Actual attempt	0			
Suicidal ideation/behavior - Suicide	0			
Non-suicidal self-injurious behavior - No	18			
Non-suicidal self-injurious behavior - Yes	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Adverse Events (AEs)

End point title	Number of Participants With Adverse Events (AEs)[2]

End point description:

Adverse events can include any of the following: clinically significant vital signs, electrocardiogram (ECG) parameters, or laboratory parameters. An AE was defined as any untoward medical occurrence that develops or worsens in severity during the conduct of a clinical study and does not necessarily have a causal relationship to the study drug. SAEs included death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, a congenital anomaly or birth defect, or an important medical event that jeopardized the participant and required medical intervention to prevent 1 of the outcomes listed in this definition. A summary of serious and non-serious AEs regardless of causality is located in 'Reported Adverse Events module'. The ITT analysis set included all enrolled participants, regardless of whether or not a participant took any TEV-50717.

End point type	Primary

End point timeframe:

Baseline up to Week 55

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: No statistical analyses were planned for this endpoint.

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: participants	39			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Extrapyramidal Symptom Rating Scale (ESRS) Subscale I Total Score at Week 54

End point title	Change From Baseline in Extrapyramidal Symptom Rating Scale (ESRS) Subscale I Total Score at Week 54[3]

End point description:

The ESRS subscale I is a 7-item subjective questionnaire to evaluate parkinsonism, akathisia, dystonia and dyskinesia. The ESRS I is scored on a 4-point scale (0=absent, 1=Mild, 2=Moderate, 3=Severe) for each item. The evaluation takes into account the verbal report of the participant on 1) the frequency and duration of the symptom during the day, 2) the number of days the symptom was present during the last week, and 3) the subjective evaluation of the intensity of the symptom by the participant. Total score was the sum of the 7 items which ranges from 0 (absent) to 28 (severe). Higher scores indicate

greater severity of disorder. The ITT analysis set included all enrolled participants, regardless of whether or not a participant took any TEV-50717. Here, 'overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Week 54

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: No statistical analyses were planned for this endpoint.

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: units on a scale				
arithmetic mean (standard deviation)	-1.4 (± 2.02)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in CBCL Syndrome Total Score at Week 53

End point title	Change From Baseline in CBCL Syndrome Total Score at Week 53[4]

End point description:

The full CBCL has two parts, a Competence Scale (Parts I to VII) and a Syndrome Scale (behavioral items). Syndrome Scale comprises 113 questions related to problem behaviors. For each item, the responses are recorded on a scale: 0 = Not True; 1 = Somewhat or Sometimes True; 2 = Very True or Often True. The problem behaviors are scored on the following 8 empirically based syndromes: anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behavior, and aggressive behavior. CBCL syndrome total score ranged from 0 (no problem) to 226 (lesser problem), which was calculated by adding individual scores of each domain. Higher scores = greater problems in child behavior. ITT analysis set = all enrolled participants, regardless of whether or not a participant took any TEV-50717. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Week 53

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: No statistical analyses were planned for this endpoint.

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: units on a scale				
arithmetic mean (standard deviation)	-1.7 (± 14.96)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Child Behavior Checklist (CBCL) Competence Total Score at Week 53

End point title	Change From Baseline in Child Behavior Checklist (CBCL) Competence Total Score at Week 53[5]

End point description:

CBCL assesses behavioral and emotional status in children ages 6 through 18 years of age as reported by the caregiver. Full CBCL has 2 parts, a Competence Scale (Parts I to VII) and a Syndrome Scale (behavioral items). Competence Scale assesses various activities (sports, hobbies, games, organizations, clubs, teams, groups, jobs, and chores), interpersonal relationships, and academic performance. Checklists having 120 questions consist of a number of statements about child's behavior and responses which are recorded on a scale: 0 = Not True; 1 = Somewhat or Sometimes True; 2 = Very True or Often True. CBCL competence total score ranged from 0 (no problem) to 240 (lesser problem), which was calculated by adding individual scores of each domain. Higher scores= greater problems in child behavior. ITT analysis set= all enrolled participants, regardless of whether or not a participant took any TEV-50717. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Week 53

Notes:

[5] - 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: No statistical analyses were planned for this endpoint.

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: units on a scale				
arithmetic mean (standard deviation)	0.49 (± 3.018)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in ESRS Subscale II Total Score at Week 54

End point title	Change From Baseline in ESRS Subscale II Total Score at Week 54[6]

End point description:

The ESRS subscale II is a 17-item questionnaire to evaluate parkinsonism and akathisia. The ESRS II consists of the following parts: tremor (0 [none]–48 [severe]), gait and posture (0 [none]–6 [severe]), postural stability (0 [none]-6 [severe]), rigidity (0 [none]–24 [severe]), expressive automatic movements (0 [none]–6 [severe]), bradykinesia (0 [none]-6 [severe]), and akathisia (0 [none]–6 [severe]). Total score was the sum of the 17 items ranging from 0 (absent) to 102 (severe). Higher scores indicate greater severity of disorder. The ITT analysis set included all enrolled participants, regardless of whether or not a participant took any TEV-50717. Here, 'overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Week 54

Notes:

[6] - 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: No statistical analyses were planned for this endpoint.

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: units on a scale				
arithmetic mean (standard deviation)	-1.5 (± 6.41)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Epworth Sleepiness Scale (ESS) Total Score at Week 54

End point title	Change From Baseline in Epworth Sleepiness Scale (ESS) Total Score at Week 54[7]

End point description:

The ESS is a self-administered questionnaire composed of 8 questions that provide a measure of a participant's general level of daytime sleepiness. The ESS is composed of 8 items. The responders were asked to rate their chances of falling asleep while engaged at 8 different activities, on a 4-point scale: 0 = would never fall asleep; 1=slight chance of falling asleep; 2=moderate chance of falling asleep; 3=high chance of falling asleep. Total score was calculated as the sum of 8 item scores ranging from 0 (never) to 24 (high chance of falling asleep). Higher scores indicate high chances of falling asleep. The ITT analysis set included all enrolled participants, regardless of whether or not a participant took any TEV-50717. Here, 'overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Week 54

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: No statistical analyses were planned for this endpoint.

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: units on a scale				
arithmetic mean (standard deviation)	0.7 (± 3.51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the MD-CRS Part II Total Score (Movement Disorder Severity, Centrally Read)

End point title	Change From Baseline in the MD-CRS Part II Total Score (Movement Disorder Severity, Centrally Read)

End point description:

MD-CRS part II evaluates severity of movement disorder on a scale of 0 to 4 in 7 body regions. All items were scored by rater and centrally read based on video recording. In rating the movement disorder, 0 refers to absence of a movement disorder and 4 refers to a situation where movement disorder is present during all the tasks for the region examined and/or involves ≥3 of other regions, making completion impossible. The 7 body regions are eye and periorbital region, face, tongue and perioral region, neck, trunk, upper limb, and lower limb. Total score was obtained by summing the individual items scores and ranges from 0 (absent of movement disorder) to 28 (marked/prolonged movement disorder). Higher scores = more movement disorder. ITT analysis set = all enrolled participants, regardless of whether or not a participant took any TEV-50717. 'Overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 53, Week 54

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Week 53 (n = 25)	-1.5 (± 3.91)			
Change at Week 54 (n = 21)	0.5 (± 4.34)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Movement Disorder-Childhood Rating Scale (MD-CRS) Part I Total Score (General Assessment, Centrally Read)

End point title	Change From Baseline in the Movement Disorder-Childhood Rating Scale (MD-CRS) Part I Total Score (General Assessment, Centrally Read)

End point description:

The MD-CRS part I evaluates the impact of dyskinesia in cerebral palsy (DCP) on the activities of the participant and provides a general assessment of the movement disorder of motor function (7 items), oral/verbal function (3 items), self-care (3 items), and attention/alertness (2 items) on a scale of 0 (present) to 4 (absent). All items were scored by the rater in the clinic and were centrally read based on video recording. The total score was obtained by summing the individual items' scores and ranges from 0 (marked/prolonged disorder) to 60 (absent of a disorder), with higher scores indicating lesser disorder. The ITT analysis set included all enrolled participants, regardless of whether or not a participant took any TEV-50717. Here, 'overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 53, Week 54

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Week 53 (n = 30)	-2.41 (± 5.240)			
Change at Week 54 (n = 25)	-1.40 (± 4.989)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the MD-CRS Part II Total Score (General Assessment, Physician Rated)

End point title	Change From Baseline in the MD-CRS Part II Total Score (General Assessment, Physician Rated)

End point description:

MD-CRS part II evaluates the severity of movement disorder on a scale of 0 to 4 in 7 body regions, all areas in which dyskinesia can be seen. In rating the movement disorder, 0 refers to absence of a movement disorder and 4 refers to a situation where movement disorder is present during all of the tasks for the region examined and/or involves 3 or more of the other regions, making completion impossible. The 7 body regions are eye and periorbital region, face, tongue and perioral region, neck, trunk, upper limb, and lower limb. Total score was obtained by summing the individual items' scores and ranges from 0 (absent of movement disorder) to 28 (marked/prolonged movement disorder), with higher scores indicating more movement disorder. ITT analysis set = all enrolled participants, regardless of whether or not a participant took any TEV-50717. 'Overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 53, Week 54

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Week 53 (n = 26)	-3.12 (± 4.255)			
Change at Week 54 (n = 24)	-1.88 (± 3.927)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the MD-CRS Part I Total Score (General Assessment, Physician Rated)

End point title	Change From Baseline in the MD-CRS Part I Total Score (General Assessment, Physician Rated)

End point description:

The MD-CRS part I evaluates the impact of DCP on the activities of the participant and provides a general assessment of the movement disorder of motor function (7 items), oral/verbal function (3 items), self-care (3 items), and attention/alertness (2 items) on a scale of 0 (present) to 4 (absent). All items were scored by the investigational center physician. The total score was obtained by summing the individual items' scores and ranges from 0 (marked/prolonged movement disorder) to 60 (absent of a movement disorder), with higher scores indicating lesser movement disorder. The ITT analysis set included all enrolled participants, regardless of whether or not a participant took any TEV-50717. Here, 'overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 53, Week 54

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Week 53 (n = 26)	-2.6 (± 3.70)			
Change at Week 54 (n = 24)	-1.4 (± 3.72)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in MD-CRS Global Index Score (Calculated From MD-CRS Parts I and II Total Scores, Physician Rated)

End point title	Change From Baseline in MD-CRS Global Index Score (Calculated From MD-CRS Parts I and II Total Scores, Physician Rated)

End point description:

MD-CRS Global Index consolidates the information from parts I and II using the method of weighted means of 2 normalized indexes obtained from each part. Standardized/normalized score for each item with value X is calculated as: Xst = X – Xmin divided by Xmax – Xmin, where Xmax is the maximum value for score, and Xmin is the minimum value for score, or 4 and 0 respectively. Normalized index for scale, MD-CRS parts I or II, Index I or II, is calculated as the mean value of Xst. MD-CRS Global index = n1 * index 1 + n2 * index 2 divided by n1 + n2, where n1 and n2 are numbers of items in MD-CRS parts I and II respectively. Minimum score = 0 (better); maximum score = 1 (worse). The higher score indicates more severe movement disorder. ITT analysis set = all enrolled participants, regardless of whether or not a participant took any TEV-50717. 'Overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 53, Week 54

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Week 53 (n = 26)	-0.1 (± 0.07)			
Change at Week 54 (n = 24)	-0.0 (± 0.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in MD-CRS Global Index Score (Calculated From MD-CRS Parts I and II Total Scores, Centrally Read)

End point title	Change From Baseline in MD-CRS Global Index Score (Calculated From MD-CRS Parts I and II Total Scores, Centrally Read)

End point description:

MD-CRS Global Index consolidates the information from parts I and II using the method of weighted means of 2 normalized indexes obtained from each part. Standardized/normalized score for each item with value X is calculated as: Xst = X – Xmin divided by Xmax – Xmin, where Xmax is the maximum value for score, and Xmin is the minimum value for score, or 4 and 0 respectively. Normalized index for scale, MD-CRS parts I or II, Index I or II, is calculated as the mean value of Xst. MD-CRS Global index = n1 * index 1 + n2 * index 2 divided by n1 + n2, where n1 and n2 are numbers of items in MD-CRS parts I and II respectively. Minimum score = 0 (better); maximum score = 1 (worse). The higher score indicates more severe movement disorder. ITT analysis set = all enrolled participants, regardless of whether or not a participant took any TEV-50717. 'Overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 53, Week 54

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Week 53 (n = 30)	-0.0 (± 0.08)			
Change at Week 54 (n= 25)	-0.0 (± 0.06)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Caregiver Global Impression of Improvement (CaGI-I) Scale Score (Global, Caregiver Rated) at Week 54

End point title	Change From Baseline in Caregiver Global Impression of Improvement (CaGI-I) Scale Score (Global, Caregiver Rated) at Week 54

End point description:

The CaGI-I is single item questionnaire to assess the caregiver's impression of improvement in dyskinesia symptoms after initiating therapy. The scale is a caregiver-reported outcome that aims to evaluate all aspects of participants' health and determine if there has been an overall improvement or not in dyskinesia symptoms. The caregiver selected the 1 response from the response options that gave the most accurate description of change in dyskinesia symptoms of the participant they cared for from the beginning of the study: 1=very much improved (since the initiation of treatment); 2=much improved; 3=minimally improved; 4=no change from baseline (symptoms remain essentially unchanged); 5=minimally worse; 6=much worse; 7=very much worse (since the initiation of treatment). ITT analysis set = all enrolled participants, regardless of whether or not a participant took any TEV-50717. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 54

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: units on a scale				
arithmetic mean (standard deviation)	-0.6 (± 1.20)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Global Impression of Improvement (CGI-I) Scale Score (Global, Physician Rated) at Week 54

End point title	Change From Baseline in Clinical Global Impression of Improvement (CGI-I) Scale Score (Global, Physician Rated) at Week 54

End point description:

CGI-I is a clinician-reported outcome that uses a 7-point Likert scale: 1=very much improved since initiation of treatment (nearly all better; good level of functioning; minimal symptoms; represents a very substantial change); 2=much improved (notably better with significant reduction of symptoms; increase in the level of functioning but some symptoms remain); 3=minimally improved (slightly better with little or no clinically meaningful reduction of symptoms); 4=no change from baseline (symptoms remain unchanged); 5=minimally worse (slightly worse but may not be clinically meaningful); 6=much worse (clinically significant increase in symptoms and diminished functioning); 7=very much worse since the initiation of treatment (severe exacerbation of symptoms and loss of functioning). ITT analysis set = all enrolled participants, regardless of whether or not a participant took any TEV-50717. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 54

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: units on a scale				
arithmetic mean (standard deviation)	-0.2 (± 0.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Global Impression of Severity (CGI-S) Scale Score (Global, Physician Rated) at Week 54

End point title	Change From Baseline in Clinical Global Impression of Severity (CGI-S) Scale Score (Global, Physician Rated) at Week 54

End point description:

CGI-S uses a 7-point Likert scale to assess dyskinesia severity as follows: 1=normal (not at all ill); 2=borderline (subtle or suspected pathology); 3=mild (clearly established symptoms with minimal, if any, distress or difficulty in social and/or occupational function); 4=moderate (overt symptoms causing noticeable, but modest, functional impairment or distress; symptom level may warrant medication); 5=marked (intrusive symptoms that distinctly impair social/occupational function or cause intrusive levels of distress); 6=severe (disruptive symptoms, behavior, and function are frequently influenced by symptoms, may require assistance from others); 7=extreme (symptoms drastically interfere in many life functions; may be hospitalized). Higher scores = more severity. ITT analysis set = all enrolled participants, regardless of whether or not a participant took any TEV-50717. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 54

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: units on a scale				
arithmetic mean (standard deviation)	-0.3 (± 0.64)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pediatric Evaluation Disability Inventory-Computer Adapted Test (PEDI-CAT) Score (Activities of Daily Living [ADL], Caregiver Completed, Content-Balanced Version) at Week 53

End point title	Change From Baseline in Pediatric Evaluation Disability

	Inventory-Computer Adapted Test (PEDI-CAT) Score (Activities of Daily Living [ADL], Caregiver Completed, Content-Balanced Version) at Week 53

End point description:

PEDI-CAT measures function in 4 domains: Daily Activities; Mobility; Social/Cognitive, and Responsibility. Content-balanced version presents a balance of items from each of the Daily Activities domain's content areas. PEDI-CAT software utilizes Item Response Theory statistical models to estimate a child's abilities from a minimal number of the most relevant items or from a set number of items within each domain. CAT program then displays results: normative standard scores, scaled scores, and SE. Scaled score is reported in this endpoint. Scaled scores are based on an estimate of the placement of an individual child along the hierarchical scale within each domain. PEDI-CAT scaled scores are on 20 (less improvement) to 80 (more improvement) scale metric. Higher scores = greater improvement. ITT analysis set = all enrolled participants, regardless of whether or not a participant took any TEV-50717. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 53

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: units on a scale				
arithmetic mean (standard deviation)	0.9 (± 2.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Unified Huntington's Disease Rating Scale-Total Maximal Chorea (UHDRS-TMC) Score (Centrally Read) at Week 53

End point title	Change From Baseline in Unified Huntington's Disease Rating Scale-Total Maximal Chorea (UHDRS-TMC) Score (Centrally Read) at Week 53

End point description:

The UHDRS-TMC is part of the Unified Huntington's Disease Rating Scale-Total Motor Score (UHDRS-TMS) assessment and assesses the severity of chorea in the 7 body parts: face, mouth, trunk, and the 4 extremities (right and left upper extremities, right and left lower extremities). Each part was rated from 0 (absent) to 4 (prolonged). The central rating was done for all participants, based on the videos collected for the central rating of MD-CRS. The TMC score was obtained by adding up each of the separate scores and ranged from 0 (absent) to 28 (marked/prolonged), with higher scores indicating the worse symptoms. The ITT analysis set included all enrolled participants, regardless of whether or not a participant took any TEV-50717. Here, 'overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 53

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: units on a scale				
arithmetic mean (standard deviation)	0.0 (± 3.20)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Unified Huntington's Disease Rating Scale-Total Motor Score (UHDRS-TMS) Score (Physician Rated) at Week 53

End point title	Change From Baseline in Unified Huntington's Disease Rating Scale-Total Motor Score (UHDRS-TMS) Score (Physician Rated) at Week 53

End point description:

The UHDRS comprises a broad assessment of features associated with Huntington's disease (HD). It is a research tool that has been developed to provide a uniform assessment of the clinical features and course of HD. The Total Motor Score assessment of the UHDRS (UHDRS-TMS) comprises 15 items and assesses eye movements, speech, alternating hand movements, dystonia, chorea, and gait. The UHDRS-TMS was calculated as the sum of the 31 motor assessments; each of which ranged between 0 (absent) to 4 (worst). All items were scored by the investigational center physician. TMS score is a sum of individual scores ranging from 0 (normal motor function) to 124 (severely impaired motor function), with lower scores indicating better motor function. The ITT analysis set included all enrolled participants, regardless of whether or not a participant took any TEV-50717. Here, 'overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 53

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: units on a scale				
arithmetic mean (standard deviation)	-7.8 (± 7.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Unified Huntington's Disease Rating Scale-Total Maximal Dystonia (UHDRS-TMD) Score (Centrally Read) at Week 53

End point title	Change From Baseline in Unified Huntington's Disease Rating Scale-Total Maximal Dystonia (UHDRS-TMD) Score (Centrally Read) at Week 53

End point description:

The UHDRS-TMD is part of the UHDRS-TMS assessment and assesses the severity of dystonia in the 5

body parts: trunk and the 4 extremities (right and left upper extremities, right and left lower extremities). Each part was rated from 0 (absent) to 4 (prolonged). The central rating was done for all participants, based on the videos collected for the central rating of MD-CRS. The TMD score was obtained by adding up each of the separate scores and ranged from 0 (absent) to 20 (marked/prolonged), with higher scores indicating the worse symptoms. The ITT analysis set included all enrolled participants, regardless of whether or not a participant took any TEV-50717. Here, 'overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 53

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: units on a scale				
arithmetic mean (standard deviation)	-1.0 (± 3.38)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Unified Huntington’s Disease Rating Scale-Total Maximal Dystonia (UHDRS-TMD) Score (Physician Rated) at Week 53

End point title	Change From Baseline in Unified Huntington’s Disease Rating Scale-Total Maximal Dystonia (UHDRS-TMD) Score (Physician Rated) at Week 53

End point description:

The UHDRS-TMD is part of the UHDRS-TMS assessment and assesses the severity of dystonia in the 5 body parts: trunk and the 4 extremities (right and left upper extremities, right and left lower extremities). Each part was rated from 0 (absent) to 4 (prolonged). All items were scored by the investigational center physician. The TMD score was obtained by adding up each of the separate scores and ranged from 0 (absent) to 20 (marked/prolonged), with higher scores indicating the worse symptoms. The ITT analysis set included all enrolled participants, regardless of whether or not a participant took any TEV-50717. Here, 'overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 53

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: units on a scale				
arithmetic mean (standard deviation)	-0.9 (± 1.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Unified Huntington's Disease Rating Scale-Total Maximal Chorea (UHDRS-TMC) Score (Physician Rated) at Week 53

End point title	Change From Baseline in Unified Huntington's Disease Rating Scale-Total Maximal Chorea (UHDRS-TMC) Score (Physician Rated) at Week 53

End point description:

The UHDRS-TMC is part of the UHDRS-TMS assessment and assesses the severity of chorea in the 7 body parts: face, mouth, trunk, and the 4 extremities (right and left upper extremities, right and left lower extremities). Each part was rated from 0 (absent) to 4 (prolonged). All items were scored by the investigational center physician. The TMC score was obtained by adding up each of the separate scores and ranged from 0 (absent) to 28 (marked/prolonged), with higher scores indicating the worse symptoms. The ITT analysis set included all enrolled participants, regardless of whether or not a participant took any TEV-50717. Here, 'overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 53

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: units on a scale				
arithmetic mean (standard deviation)	-3.9 (± 4.50)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Canadian Occupational Performance Measure (COPM) (Physician Rated) Score at Week 53

End point title	Change From Baseline in Canadian Occupational Performance Measure (COPM) (Physician Rated) Score at Week 53

End point description:

The COPM, a semi-structured interview, was used to assess a participant's perception of performance in the areas of self-care, productivity and leisure. The COPM involves a 5-step process within a semi-structured interview conducted by a therapist. The participants were asked to rate 5 most important activities on a 10-point scale for performance and satisfaction, ranging from 1 (not at all able/satisfied) to 10 (able to perform extremely well/ extremely satisfied). Higher scores indicated very good performance and high satisfaction. The ITT analysis set included all enrolled participants, regardless of whether or not a participant took any TEV-50717. Here, 'overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 53

End point values	TEV-50717			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: units on a scale				
arithmetic mean (standard deviation)	1.4 (± 1.36)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 55

Adverse event reporting additional description:

The ITT analysis set included all enrolled participants, regardless of whether or not a participant took any TEV-50717.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	TEV-50717

Reporting group description:

TEV-50717 was administered as oral tablets once daily for up to 53 weeks (7 weeks dose titration and 46 weeks maintenance). From Week 1 through Week 7, the dose of TEV-50717 was adjusted according to the titrations scheme (based on body weight and CYP2D6 impairment status at baseline) to identify a dose level that optimally reduced dyskinesia (as determined by the investigator, as indicated by a reduction in the CGI-I) and was well tolerated. After titration, participants continued to receive their maintenance dose over the next 46 weeks.

Serious adverse events	TEV-50717		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 44 (2.27%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Cardiac disorders			
Cardiopulmonary failure			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
COVID-19			

subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	TEV-50717		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 44 (75.00%)		
Nervous system disorders			
Akathisia			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	4		
Dystonia			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	7		
Headache			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		
Somnolence			
subjects affected / exposed	21 / 44 (47.73%)		
occurrences (all)	32		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	5		
Fatigue			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	4		
Diarrhoea			
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	4		

Constipation subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all)	3 / 44 (6.82%) 3 3 / 44 (6.82%) 6		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	3 / 44 (6.82%) 5		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) COVID-19 subjects affected / exposed occurrences (all)	3 / 44 (6.82%) 3 4 / 44 (9.09%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 October 2019	The following major procedural changes (not all-inclusive) were made to the protocol: • Clarified in tables, text, and appendices which data from assessments at Weeks 15 and 16 of the parent Study TV50717-CNS-30080 could be used as study Day 1 of Study TV50717-CNS-30081 and which assessments needed to be repeated on study Day 1. • Clarified that assessment of MD-CRS part II items was to be based solely on chorea in this study. • Added beta-human chorionic gonadotropin (β-HCG) test in urine at Week 54 for females who were postmenarchal or ≥12 years of age at study Day 1. • Revised guidance on dose adjustments for temporary suspension of study drug. • Added reasons to discontinue participants from the study: diminished hepatic function with definitions provided and development of neuroleptic malignant syndrome. • Added investigator's responsibility to manage participant's condition and suspension of treatment if participant's serum potassium or magnesium falls below the lower limit of normal. • Allowed use of cannabis or formulations or derivatives of cannabis in relatively stable amounts, for medical purposes (where applicable according to local regulation), under the guidance, supervision, or prescription of a clinician. • Revised the dose strengths available for use in the study, the appearance of the tablets, and the number of tablets per bottle. • Changed the use of parent/caregiver to caregiver throughout the protocol.
19 March 2020	The following major procedural changes (not all-inclusive) were made to the protocol: • Added 2 secondary objectives: UHDRS-TMC and UHDRS-TMD (both physician rated). • Revised the enrollment period such that participants can either enroll in the study at the Week 16 visit of Study TV50717-CNS-30080, between 2 and ≤4 weeks after the Week 15 visit or more than 4 weeks up to 6 months following the Week 15 visit of Study TV50717-CNS-30080; the timing of enrollment determined the assessments to be performed at the initial study visit. • Clarified that participants were classified as CYP2D6-impaired if they were receiving a strong CYP2D6 inhibitor. • Clarified that participant age at enrollment into the study was the age at the time of their enrollment in the parent study and noted that some participants who were greater than 18 years would use scales designated for participants up to 18 years old. • Clarified the number of days permitted between dose increases based on weight. • Revised various exclusion criteria to provide guidance to the investigator concerning the order of administration and review of the assessment scales. • Revised exclusion criteria to provide clearer guidelines for participant exclusion, clarified concomitant medications, and removed exclusion criteria surrounding botulinum neurotoxin. • Clarified urine drug screen exclusion criteria and assessment. • Clarified participant withdrawal criteria • Clarified administration of TEV-50717 and study drug storage stipulations. • Prior use of antipsychotic drugs were allowed under conditions specified in the protocol. • Increased blood draws by approximately 4 mL. • Added text on administration of β-HCG tests. • Added guidance on ECG to the investigator with regard to participant eligibility.
23 June 2020	The following major procedural changes (not all-inclusive) were made to the protocol: • Added video recording of the MD-CRS assessment because it is a recognized component of the MD CRS. • Added an appendix which provided management of COVID-19 pandemic-related operations. • Clarified vital signs assessments used for study Day 1. • Increased blood draws by approximately 1.5 mL. • Revised stimulant medications that may be allowed in urine drug screen.

01 June 2022	The following major procedural changes (not all-inclusive) were made to the protocol: • Added 4 secondary endpoints: MD-CRS part I and part II total scores (centrally read) and UHDRS-TMC and UHDRS-TMD (centrally read), and text to describe blinded central video review. • Reduced the time period in which participants can enroll following the end of Study TV50717 CNS 30080 from 6 months to 4 weeks. • Revised text to account for the change in sample size (from up to a maximum of 230 participants to approximately 45 participants) based on the number of participants in parent Study TV50717-CNS-30080. • Removed the second interim analysis. • Clarified procedures for monitoring participant compliance with study drug. • Clarified participant and/or caregiver responsibilities for completion of the ESS depending on participant age. • Added ECG types and review processes.

Notes:

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.

The study was terminated early due to failure of TV50717-CNS-30080 (parent study) to meet the primary efficacy endpoint.

Notes: