Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Safety, Efficacy and Pharmacodynamic Study of Basmisanil (RO5186582) in Adults with Severe Motor Impairment Following an Ischemic Stroke

Summary

EudraCT number	2015-003227-66
Trial protocol	ES
Global end of trial date	03 November 2017

Results information

Result version number	v1 (current)
This version publication date	08 November 2018
First version publication date	08 November 2018

Trial information

Trial identification

Sponsor protocol code	BP29937

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02928393
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 November 2017
Global end of trial reached?	Yes
Global end of trial date	03 November 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this Phase IIa, randomized, double-blind, placebo-controlled, parallel group study was to evaluate the safety, efficacy and pharmacodynamics of basmisanil in adult participants with severe motor impairment following an ischemic stroke.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 February 2017
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	Spain: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	3
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study population consisted of male and female subjects aged 40-85 years with severe motor impairment following an acute middle cerebral artery (MCA) ischemic stroke and was conducted across three sites in Spain.

Pre-assignment

Screening details:

Male and female subjects between 40-85 years old that had an acute middle cerebral artery (MCA) ischemic stroke within 3-4 days of study enrollment were eligible for the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Basmisanil

Arm description:

Subjects received 240 milligrams (mg) of basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days.

Arm type	Experimental
Investigational medicinal product name	Basmisanil
Investigational medicinal product code	
Other name	RO5186582
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Subjects received 240 mg of basmisanil, taken orally, twice-daily (morning and evening), within 30 minutes of a meal for 90 days.

Arm title	Placebo

Arm description:

Subjects received the placebo equivalent to basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days.

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

Dosage and administration details:

Subjects received two stick packs of placebo, taken orally, twice daily (morning and evening), within 30 minutes of a meal for 90 days.

Number of subjects in period 1	Basmisanil	Placebo
Started	3	2
Completed	3	2

Baseline characteristics

Reporting groups	
Reporting group title	Basmisanil
Reporting group description:	
Subjects received 240 milligrams (mg) of basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days.	
Reporting group title	Placebo
Reporting group description:	
Subjects received the placebo equivalent to basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days.	

Reporting group values	Basmisanil	Placebo	Total
Number of subjects	3	2	5
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	59.3	66.0	
standard deviation	± 11.8	± 5.7	-
Gender Categorical Units: Subjects			
Male	3	2	5
Female	0	0	0
Race (NIH/OMB) Units: Subjects			
White	2	2	4
Unknown	1	0	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	0	2
Not Hispanic or Latino	1	0	1
Not Stated	0	2	2

Subject analysis sets	
Subject analysis set title	Basmisanil A
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All study subjects were included in the safety and efficacy analyses.	
Subject analysis set title	Basmisanil B
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All study subjects were included in the safety and efficacy analyses.	
Subject analysis set title	Basmisanil C
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All study subjects were included in the safety and efficacy analyses.	

Subject analysis set title	Placebo A
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All study subjects were included in the safety and efficacy analyses.

Subject analysis set title	Placebo B
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All study subjects were included in the safety and efficacy analyses.

Reporting group values	Basmisanil A	Basmisanil B	Basmisanil C
Number of subjects	1	1	1
Age Categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	±	±	±
Gender Categorical Units: Subjects			
Male	1	1	1
Female	0	0	0
Race (NIH/OMB) Units: Subjects			
White	1	0	1
Unknown	0	1	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	0	1	0
Not Stated	0	0	0

Reporting group values	Placebo A	Placebo B	
Number of subjects	1	1	
Age Categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	±	±	
Gender Categorical Units: Subjects			
Male	1	1	
Female	0	0	
Race (NIH/OMB) Units: Subjects			
White	1	1	
Unknown	0	0	
Ethnicity (NIH/OMB) Units: Subjects			

Hispanic or Latino	0	0	
Not Hispanic or Latino	0	0	
Not Stated	1	1	

End points

End points reporting groups

Reporting group title	Basmisanil
Reporting group description:	
Subjects received 240 milligrams (mg) of basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days.	
Reporting group title	Placebo
Reporting group description:	
Subjects received the placebo equivalent to basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days.	
Subject analysis set title	Basmisanil A
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All study subjects were included in the safety and efficacy analyses.	
Subject analysis set title	Basmisanil B
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All study subjects were included in the safety and efficacy analyses.	
Subject analysis set title	Basmisanil C
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All study subjects were included in the safety and efficacy analyses.	
Subject analysis set title	Placebo A
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All study subjects were included in the safety and efficacy analyses.	
Subject analysis set title	Placebo B
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All study subjects were included in the safety and efficacy analyses.	

Primary: Change from Baseline in Fugl-Meyer Motor Scale (FMMS) Total Score at Day 90

End point title	Change from Baseline in Fugl-Meyer Motor Scale (FMMS) Total Score at Day 90[1]
End point description:	
The FMMS is a subscale of the Fugl-Meyer Assessment (FMA) scale used to evaluate and measure recovery of motor function in post-stroke participants. The subscale contains 33 items to assess upper extremity function, and 17 items to assess lower extremity function. Each item is scored on a 3-point scale, where 0 means an item cannot be performed, 1 means an item can be partially performed, and 2 means an item may be fully performed. The maximum score is 66 for upper limbs and 34 for lower limbs.	
End point type	Primary
End point timeframe:	
Baseline (Day 1), Day 90	

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: Statistical analyses were not performed due to low enrollment and early study termination.

End point values	Basmisanil	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: None				
arithmetic mean (standard deviation)				
Baseline (Day 1) Day 90	29.33 (± 5.69) 56.33 (± 14.19)	30.50 (± 3.54) 60.00 (± 2.83)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Adverse Events

End point title	Number of Subjects with Adverse Events[2]

End point description:

An adverse event is any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered to be adverse

End point type	Primary

End point timeframe:

Baseline (Day 1) up to 28 days after last dose of study drug

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: Statistical analyses were not performed due to low enrollment and early study termination.

End point values	Basmisanil	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: Subjects	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in National Institute of Health Stroke Scale (NIHSS) Score

End point title	Change from Baseline in National Institute of Health Stroke Scale (NIHSS) Score[3]

End point description:

NIHSS: The NIHSS is an 11-item scale administered to all study subjects developed to assess function and degree of impairment in acute post-stroke subjects. The scale contains 11 elements rating the ability to respond to questions and to obey simple commands, eye gaze, vision, facial palsy, motor function, ataxia, sensation, language, articulation, and attention. Each element is scored between 0 and 4, with 0 indicating normal function and 4 indicating complete impairment. The highest score possible is 42.

End point type	Primary

End point timeframe:

Baseline (Day 1), Days 3, 10, 30, 90, and at follow-up

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: Statistical analyses were not performed due to low enrollment and early study termination.

End point values	Basmisanil A	Basmisanil B	Basmisanil C	Placebo A
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	1	1	1
Units: None				
number (not applicable)				
Baseline (Day 1)	9	10	9	14
Change from Baseline at Day 3	-1	-2	-3	-3
Change from Baseline at Day 10	-1	-4	-4	-6
Change from Baseline at Day 30	-3	-5	-5	-9
Change from Baseline at Day 90	-4	-8	-6	-9
Change from Baseline at Follow-Up	-1	-8	-6	-11

End point values	Placebo B			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: None				
number (not applicable)				
Baseline (Day 1)	7			
Change from Baseline at Day 3	-1			
Change from Baseline at Day 10	-3			
Change from Baseline at Day 30	-3			
Change from Baseline at Day 90	-6			
Change from Baseline at Follow-Up	-6			

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Montreal Cognitive Assessment (MoCA) Score

End point title	Change from Baseline in Montreal Cognitive Assessment (MoCA) Score[4]

End point description:

The MoCA is a screening tool used to detect mild cognitive impairment in patients with dementia or stroke. Points are given for tasks completed in the following domains: visuospatial, naming, memory, attention, language, abstraction, delayed recall, and orientation. The maximum score is 30, with higher scores indicating higher ability to complete the administered tasks. Subjects unable to complete the written portion of the tool due to hemiplegia are scored on a modified scale. 99999 = N/A

End point type	Primary

End point timeframe:

Baseline (Day 1), Days 30 and 90

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: Statistical analyses were not performed due to low enrollment and early study termination.

End point values	Basmisanil A	Basmisanil B	Basmisanil C	Placebo A
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1[5]	1	1	1
Units: None				
number (not applicable)				
Score at Baseline (Day 1)	99999	27	26	5
Score at Day 30	11	28	28	8
Score at Day 90	99999	27	28	8

Notes:

[5] - A baseline (day 1) score was not reported.

End point values	Placebo B			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: None				
number (not applicable)				
Score at Baseline (Day 1)	15			
Score at Day 30	25			
Score at Day 90	26			

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Columbia-Suicide Severity Rating Scale (C-SSRS) Scores

End point title	Change from Baseline in Columbia-Suicide Severity Rating Scale (C-SSRS) Scores[6]

End point description:

The C-SSRS is used to assess the lifetime suicidality of a subject (taken at baseline), and new instances of suicidal ideation that may occur during the study (measured for each time period since the last study visit). Subjects are rated on a scale ranging from a "wish to die" to "active suicidal thought with plan and intent."

End point type	Primary

End point timeframe:

Baseline (Day 1), Days 3, 30, 60, 90, and 28 days after the last dose of study drug

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: Statistical analyses were not performed due to low enrollment and early study termination.

End point values	Basmisanil A	Basmisanil B	Basmisanil C	Placebo A
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	1	1	1
Units: Subjects				
number (not applicable)				
Suicidal Ideation	0	0	0	0
Suicidal Ideation - Lifetime	0	0	0	0
Suicidal Ideation - Past 6 Months	0	0	0	0
Suicidal Behavior	0	0	0	0
Suicidal Behavior - Lifetime	0	0	0	0

End point values	Placebo B			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: Subjects				
number (not applicable)				
Suicidal Ideation	0			
Suicidal Ideation - Lifetime	0			
Suicidal Ideation - Past 6 Months	0			
Suicidal Behavior	0			
Suicidal Behavior - Lifetime	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fugl-Meyer Assessment (FMA) Total Score at Day 90

End point title	Change from Baseline in Fugl-Meyer Assessment (FMA) Total Score at Day 90

End point description:

The FMA is a scale used to evaluate and measure recovery in post-stroke participants across five domains - motor function, sensory function, balance, range of motion, and joint pain. Items are scored on a 3-point scale, where 0 means an item cannot be performed, 1 means an item can be partially performed, and 2 means an item may be fully performed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Day 90

End point values	Basmisanil A	Basmisanil B	Basmisanil C	Placebo A
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	1	1	1
Units: None				
Baseline (Day 1)	129	135	145	139
Change from Baseline at Day 90	69	49	80	76

End point values	Placebo B			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: None				
Baseline (Day 1)	142			
Change from Baseline at Day 90	69			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in FMA Subscale Score at Day 90

End point title	Change from Baseline in FMA Subscale Score at Day 90

End point description:

The FMA is a scale used to evaluate and measure recovery in post-stroke participants across five domains - motor function, sensory function, balance, range of motion, and joint pain. Items are scored on a 3-point scale, where 0 means an item cannot be performed, 1 means an item can be partially performed, and 2 means an item may be fully performed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Day 90

End point values	Basmisanil A	Basmisanil B	Basmisanil C	Placebo A
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	1	1	1
Units: None				
number (not applicable)				
Baseline (Day 1) FM Balance Scale Score	4	0	2	4
Change in FM Balance Score, Day 90	6	11	11	10
Baseline (Day 1) FM Sensation Scale Score	3	24	24	18
Change in FM Sensation Score, Day 90	7	0	0	2
Baseline (Day 1) FM Pain Assessment Scale Score	44	44	44	44
Change in FM Pain Assessment Score, Day 90	-3	0	0	0

Baseline (Day 1) FM Range of Motion Scale Score	44	44	44	40
Change in FM Range of Motion Score, Day 90	0	-3	0	2

End point values	Placebo B			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: None				
number (not applicable)				
Baseline (Day 1) FM Balance Scale Score	2			
Change in FM Balance Score, Day 90	11			
Baseline (Day 1) FM Sensation Scale Score	24			
Change in FM Sensation Score, Day 90	0			
Baseline (Day 1) FM Pain Assessment Scale Score	44			
Change in FM Pain Assessment Score, Day 90	0			
Baseline (Day 1) FM Range of Motion Scale Score	44			
Change in FM Range of Motion Score, Day 90	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Modified Rankin Scale (mRS) Score at Day 90

End point title	Change from Baseline in Modified Rankin Scale (mRS) Score at Day 90

End point description:

The mRS is a single-item scale used to measure the degree of functional independence and is commonly used with stroke patients. Subjects were rated on a scale of 1-5, as follows: 1 = No significant disability; 2 = Slight disability; 3= Moderate disability; 4 = Moderately severe disability; 5 = Severe disability.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Day 90

End point values	Basmisanil A	Basmisanil B	Basmisanil C	Placebo A
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	1	1	1
Units: None				
number (not applicable)				
Baseline (Day 1)	4	4	5	4
Day 90/Early Termination	3	3	2	3

Change from Baseline at Day 90	-1	-1	-3	-1

End point values	Placebo B			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: None				
number (not applicable)				
Baseline (Day 1)	4			
Day 90/Early Termination	1			
Change from Baseline at Day 90	-3			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Basmisanil (RO5185682)

End point title	Plasma Concentration of Basmisanil (RO5185682)

End point description:

Pharmacokinetic (PK) sampling was done for all subjects that received basmisanil (RO5185862).

End point type	Secondary

End point timeframe:

Days 1, 3, 10, 30, and 90

End point values	Basmisanil A	Basmisanil B	Basmisanil C	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[7]	1	1[8]	
Units: ng/mL				
number (not applicable)				
Day 1, Hour 4	1280	2690	1020	
Day 1, Hour 8	776	1820	2490	
Day 3, Pre-Dose	2170	2460	3870	
Day 3, Hour 4	3480	3290	3210	
Day 10, Pre-Dose	2810	3440	2050	
Day 30, Pre-Dose	3660	4100	3290	
Day 90	3700	9630	3480	

Notes:

[7] - 99999 = No value reported for time point

[8] - 99999 = No value reported for time point

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Infarct Lesion Volume as Determined by Magnetic Resonance Imaging (MRI)

End point title	Change in Infarct Lesion Volume as Determined by Magnetic Resonance Imaging (MRI)

End point description:

Infarct lesion volume was monitored using MRI. Baseline lesion measurements occurred approximately 5-7 after the stroke event.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 3 and 90

End point values	Basmisanil A	Basmisanil B	Basmisanil C	Placebo A
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	1	1	1
Units: Cubic millimeters (mm3)				
number (not applicable)				
Baseline Infarct Volume	1492.19	23678.26	3225.33	90212.7
Change from Baseline in Infarct Volume at Day 3	320.62	-3036.44	-743.77	-7833.17
Change from Baseline in Infarct Volume at Day 90	1179.37	-1867.85	634.3	10402.38

End point values	Placebo B			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: Cubic millimeters (mm3)				
number (not applicable)				
Baseline Infarct Volume	31456.58			
Change from Baseline in Infarct Volume at Day 3	-1805.62			
Change from Baseline in Infarct Volume at Day 90	-14827.85			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From Baseline (Day 1) up to 28 days after last dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received the placebo equivalent to basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days.	
Reporting group title	Basmisanil
Reporting group description:	
Subjects received 240 mg of basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days.	

Serious adverse events	Placebo	Basmisanil	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Placebo	Basmisanil	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	1 / 3 (33.33%)	
Eye disorders			
Dacryocystitis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			

Metatarsalgia subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 3 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2016	Removed references to health authorities outside the area of study conduct; replaced Joint Monitoring Committee (JMC) with independent data monitoring committee (iDMC); clarified methods permitted to record body temperature; made Day 1 PK sample collection optional.
24 July 2017	Expanded subject population; clarified discontinuation criteria; modified interim analysis; modified caregiver eligibility requirement; clarified assessment schedule.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
03 November 2017	The study was prematurely terminated by the sponsor due to low enrollment.	-

Notes:

Limitations and caveats

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

The low number of subjects enrolled in the study limits conclusions that may be derived from the study data.

Notes: