EU Clinical Trials Register

Clinical trial results:
A Single-arm Uncontrolled 12-month Clinical Study to Evaluate the Safety and Efficacy of
Miglustat (Zavesca®) for the Treatment of Niemann-Pick Disease Type C (NPC) in Chinese Subjects

Summary

EudraCT number	2022-002514-16
Trial protocol	Outside EU/EEA
Global end of trial date	29 March 2022

Results information

Result version number	v1 (current)
This version publication date	28 December 2022
First version publication date	28 December 2022

Trial information

Trial identification

Sponsor protocol code	AC-056C405

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03910621
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Actelion Pharmaceuticals Trading (Shanghai) Co., Ltd
Sponsor organisation address	Suite 2002-2003, Henderson 688, No. 688 West Nanjing Road, Shanghai, China, 200041
Public contact	Clinical Registry Group, Actelion Pharmaceuticals Trading (Shanghai) Co., Ltd, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Actelion Pharmaceuticals Trading (Shanghai) Co., Ltd, ClinicalTrialsEU@its.jnj.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	29 March 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the efficacy of miglustat on the rate of disease progression and disease stabilization in subjects with Niemann-Pick Disease Type C (NPC).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 April 2020
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	China: 17
Worldwide total number of subjects	17
EEA total number of subjects	0

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)	5
Adolescents (12-17 years)	7
Adults (18-64 years)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Out of the 17 enrolled subjects, 14 subjects completed the study.

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	Miglustat

Arm description:

Adult and pediatric subjects aged 4 years and older, with established diagnosis of niemann-pick disease type C (NPC) were enrolled and recieved miglustat 200 miligrams (mg) from Day 1 through Week 52. Adult subjects received miglustat 200 mg thrice daily (t.i.d), while for subjects with mild renal impairment, the starting dose was 200 mg twice daily (b.i.d) and for moderate renal impairment, the starting dose was 200 mg once daily. For subjects with NPC less than 12 years of age, dosage regimen (0.2 grams [g] t.i.d, 0.2 g b.i.d, 0.1 g t.i.d, 0.1 g b.i.d, and 0.1 g once daily) was adjusted based on body surface area (BSA).

Arm type	Experimental
Investigational medicinal product name	Miglustat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Miglustat 200 mg was administered t.i.d from Day 1 through Week 52. The recommended dose was 200 mg t.i.d. and adjusted according to BSA for children less than 12 years of age.

Number of subjects in period 1	Miglustat
Started	17
Completed	14
Not completed	3
Consent withdrawn by subject	1
Death	2

Baseline characteristics

Reporting groups

Reporting group title	Miglustat

Reporting group description:

Adult and pediatric subjects aged 4 years and older, with established diagnosis of niemann-pick disease type C (NPC) were enrolled and recieved miglustat 200 miligrams (mg) from Day 1 through Week 52. Adult subjects received miglustat 200 mg thrice daily (t.i.d), while for subjects with mild renal impairment, the starting dose was 200 mg twice daily (b.i.d) and for moderate renal impairment, the starting dose was 200 mg once daily. For subjects with NPC less than 12 years of age, dosage regimen (0.2 grams [g] t.i.d, 0.2 g b.i.d, 0.1 g t.i.d, 0.1 g b.i.d, and 0.1 g once daily) was adjusted based on body surface area (BSA).

Reporting group values	Miglustat	Total	
Number of subjects	17	17	
Age Categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	5	5	
Adolescents (12-17 years)	7	7	
Adults (18-64 years)	5	5	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	15.1		
standard deviation	± 6.56	-	
Gender Categorical			
Units: Subjects			
Female	8	8	
Male	9	9	

End points

End points reporting groups

Reporting group title	Miglustat

Reporting group description:

Adult and pediatric subjects aged 4 years and older, with established diagnosis of niemann-pick disease type C (NPC) were enrolled and recieved miglustat 200 miligrams (mg) from Day 1 through Week 52. Adult subjects received miglustat 200 mg thrice daily (t.i.d), while for subjects with mild renal impairment, the starting dose was 200 mg twice daily (b.i.d) and for moderate renal impairment, the starting dose was 200 mg once daily. For subjects with NPC less than 12 years of age, dosage regimen (0.2 grams [g] t.i.d, 0.2 g b.i.d, 0.1 g t.i.d, 0.1 g b.i.d, and 0.1 g once daily) was adjusted based on body surface area (BSA).

Primary: Change From Baseline to Week 52 in Horizontal Saccadic Eye Movement (HSEM) as Measured by Saccadic Peak Acceleration

End point title	Change From Baseline to Week 52 in Horizontal Saccadic Eye Movement (HSEM) as Measured by Saccadic Peak Acceleration[1]

End point description:

Change from baseline to Week 52 in HSEM as measured by saccadic peak acceleration was reported. Saccadic eye movements (SEM) were rapid eye movements under voluntary control (including saccade initiation, speed and extent) that were essential for the normal shifting of focus from one object to another within the visual field. Full analysis set included all enrolled subjects who completed the screening period. Here, 'N' (number of subjects analysed) signifies number of subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline to Week 52

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 inferential statistics was planned for this primary endpoint.

End point values	Miglustat			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: degree per square second (deg/sec^2)				
arithmetic mean (standard deviation)	2900.42 (± 1923.432)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline to Week 52 in HSEM as Measured by Mean Velocity

End point title	Change From Baseline to Week 52 in HSEM as Measured by Mean Velocity[2]

End point description:

Change from baseline to Week 52 in HSEM as measured by mean velocity was reported. SEM were rapid eye movements under voluntary control (including saccade initiation, speed and extent) that were

essential for the normal shifting of focus from one object to another within the visual field. Full analysis set included all enrolled subjects who completed the screening period. Here, 'N' (number of subjects analysed) signifies number of subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:	
Baseline to Week 52	

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 inferential statistics was planned for this primary endpoint.

End point values	Miglustat			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: degree per second (deg/sec)				
arithmetic mean (standard deviation)	8.745 (± 21.3558)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline to Week 52 in HSEM as Measured by Peak Duration

End point title	Change From Baseline to Week 52 in HSEM as Measured by Peak Duration[3]

End point description:

Change from baseline to Week 52 in HSEM as measured by peak duration was reported. SEM were rapid eye movements under voluntary control (including saccade initiation, speed and extent) that were essential for the normal shifting of focus from one object to another within the visual field. Full analysis set included all enrolled subjects who completed the screening period. Here, 'N' (number of subjects analysed) signifies number of subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:	
Baseline to Week 52	

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 inferential statistics was planned for this primary endpoint.

End point values	Miglustat			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: sec				
arithmetic mean (standard deviation)	-4.074 (± 11.3309)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline to Week 52 in HSEM as Measured by Linear Regression Slopes

End point title	Change From Baseline to Week 52 in HSEM as Measured by Linear Regression Slopes[4]

End point description:

Change from baseline to Week 52 in HSEM as measured by linear regression slopes was reported. SEM were rapid eye movements under voluntary control (including saccade initiation, speed and extent) that were essential for the normal shifting of focus from one object to another within the visual field. Full analysis set included all enrolled subjects who completed the screening period. Here, 'N' (number of subjects analysed) signifies number of subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline to Week 52

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 inferential statistics was planned for this primary endpoint.

End point values	Miglustat			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: ms per degree				
arithmetic mean (standard deviation)	0.173 (± 2.0256)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline to Week 52 in HSEM as Measured by Line Slopes

End point title	Change From Baseline to Week 52 in HSEM as Measured by Line Slopes[5]

End point description:

Change from baseline to Week 52 in HSEM as measured by line slopes was reported. SEM were rapid eye movements under voluntary control (including saccade initiation, speed and extent) that were essential for the normal shifting of focus from one object to another within the visual field. Full analysis set included all enrolled subjects who completed the screening period. Here, 'N' (number of subjects analysed) signifies number of subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline to Week 52

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 inferential statistics was planned for this primary endpoint.

End point values	Miglustat			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: ms/degree				
arithmetic mean (standard deviation)	0.173 (± 2.0256)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Week 26 and Week 52 in Pineda Disability Scale Score

End point title	Change From Baseline to Week 26 and Week 52 in Pineda Disability Scale Score

End point description:

Change form baseline to Week 26 and Week 52 in pineda disability scale score was reported. The changes in Pineda disability scale was a total additive score of 6 items which included ambulation ranged from 1(clumsy)-5(wheelchair-bound), manipulation ranged from 1(tremor)-4(severe dysmetria/dystonia), language ranged from 1(delayed acquisitions)-5(absence of communication), swallowing ranged from 1(abnormal chewing)-4(nasogastric/gastric button feeding), seizures ranged from 1(occasional seizures)-3(seizures resistant to antiepileptic drugs), and ocular movements ranged from 1(slow ocular pursuit)-3(complete ophthalmoplegia). The total score ranged from 0-24, where higher score indicates poorer condition. Full analysis set included all enrolled subjects who completed the screening period. Here, 'N'(number of subjects analysed) signifies number of subjects who were evaluable for this endpoint and 'n'(number analysed) signifies number of subjects evaluable at the specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Week 26, and Week 52

End point values	Miglustat			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: units on a scale				
arithmetic mean (standard deviation)				
Ambulation: Week 26 (n=14)	0.0 (± 0.39)			
Ambulation: Week 52 (n=12)	0.0 (± 0.43)			
Manipulation: Week 26 (n=14)	0.0 (± 0.55)			
Manipulation: Week 52 (n=12)	-0.1 (± 0.79)			
Language: Week 26 (n=14)	-0.1 (± 0.27)			
Language: Week 52 (n=12)	-0.1 (± 0.29)			
Swallowing: Week 26 (n=14)	-0.6 (± 0.76)			
Swallowing: Week 52 (n=12)	-0.4 (± 0.79)			
Seizures: Week 26 (n=14)	-0.1 (± 0.62)			
Seizures: Week 52 (n=12)	-0.2 (± 0.58)			
Ocular Movements: Week 26 (n=14)	-0.2 (± 0.43)			
Ocular Movements: Week 52 (n=12)	-0.4 (± 0.51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Number of Subjects with Treatment-emergent Serious Adverse Events (TESAEs)

End point description:

A SAE is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. An AE is any untoward medical occurrence, i.e., any unfavorable and unintended sign, including an abnormal laboratory finding, symptom, or disease that occurs in a subject during the course of the study, whether or not considered by the investigator as related to study treatment. Treatment-emergent SAEs are defined as serious events between administration of study drug and after the last dose that were absent before treatment or that worsen relative to pretreatment state. The safety set (SS) included all subjects who received at least one dose of miglustat.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Miglustat			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: subjects	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects with Treatment-emergent Adverse Events (TEAEs)

End point description:

An AE was any untoward medical occurrence, that was, any unfavorable and unintended sign, including an abnormal laboratory finding, symptom, or disease that occurs in a subject during the course of the study, whether or not considered by the investigator as related to study treatment. TEAE was any AE temporally associated with the use of study treatment (from study treatment initiation until 30 days after study treatment discontinuation) whether or not considered by the investigator as related to study treatment. The safety set (SS) included all subjects who received at least one dose of miglustat.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Miglustat			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: subjects	17			

Statistical analyses

No statistical analyses for this end point

End point values	Miglustat			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: subjects	17			

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 52 weeks for serious and other (non-serious) adverse events and up to 56 weeks for all-cause mortality

Adverse event reporting additional description:

The safety set (SS) included all subjects who received at least one dose of miglustat.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Miglustat

Reporting group description:

Adult and pediatric subjects aged 4 years and older, with established diagnosis of niemann-pick disease type C (NPC) were enrolled and recieved miglustat 200 miligrams (mg) from Day 1 through Week 52. Adult subjects received miglustat 200 mg thrice daily (t.i.d), while for subjects with mild renal impairment, the starting dose was 200 mg twice daily (b.i.d) and for moderate renal impairment, the starting dose was 200 mg once daily. For subjects with NPC less than 12 years of age, dosage regimen (0.2 grams [g] t.i.d, 0.2 g b.i.d, 0.1 g t.i.d, 0.1 g b.i.d, and 0.1 g once daily) was adjusted based on body surface area (BSA).

Serious adverse events	Miglustat		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 17 (29.41%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Accidental death	Additional description: Accidental death		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Asphyxia	Additional description: Asphyxia		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Skin and subcutaneous tissue disorders			
Henoch-Schonlein purpura	Additional description: Henoch-Schonlein purpura		

subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Malnutrition	Additional description: Malnutrition		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Miglustat		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)		
General disorders and administration site conditions			
Influenza like illness	Additional description: Influenza like illness		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Menstrual disorder	Additional description: Menstrual disorder		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	9		
Psychiatric disorders			

Insomnia	Additional description: Insomnia		
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Mental disorder	Additional description: Mental disorder		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Investigations			
Blood potassium increased	Additional description: Blood potassium increased		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Weight decreased	Additional description: Weight decreased		
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Ligament sprain	Additional description: Ligament sprain		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Congenital, familial and genetic disorders			
Niemann-Pick disease	Additional description: Niemann-Pick disease		
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Nervous system disorders			
Amnesia	Additional description: Amnesia		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Dizziness	Additional description: Dizziness		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Epilepsy	Additional description: Epilepsy		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Muscle tone disorder	Additional description: Muscle tone disorder		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Paraesthesia	Additional description: Paraesthesia		

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

Tremor

Additional description: Tremor

subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		

Blood and lymphatic system disorders

Leukocytosis

Additional description: Leukocytosis

subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		

Neutrophilia

Additional description: Neutrophilia

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

Thrombocytopenia

Additional description: Thrombocytopenia

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

Ear and labyrinth disorders

Vertigo

Additional description: Vertigo

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		

Gastrointestinal disorders

Anal incontinence

Additional description: Anal incontinence

subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	7		

Abdominal pain

Additional description: Abdominal pain

subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	3		

Diarrhoea

Additional description: Diarrhoea

subjects affected / exposed	12 / 17 (70.59%)		
occurrences (all)	24		

Haemorrhoids

Additional description: Haemorrhoids

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

Mouth ulceration

Additional description: Mouth ulceration

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

Nausea

Additional description: Nausea

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Vomiting	Additional description: Vomiting		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hepatic function abnormal	Additional description: Hepatic function abnormal		
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Eczema	Additional description: Eczema		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Henoch-Schonlein purpura	Additional description: Henoch-Schonlein purpura		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Renal and urinary disorders			
Haematuria	Additional description: Haematuria		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Infections and infestations			
Large intestine infection	Additional description: Large intestine infection		
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Tonsillitis	Additional description: Tonsillitis		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	7 / 17 (41.18%)		
occurrences (all)	18		
Metabolism and nutrition disorders			

Hyperuricaemia	Additional description: Hyperuricaemia		
subjects affected / exposed	4 / 17 (23.53%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 March 2020	The purpose of this amendment was to add an additional choice of laboratory for genetic test that confirms the Niemann-Pick Disease Type C (NPC) disease diagnosis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported