Clinical trial results:
A Multicenter, Open-label Extension Study to Evaluate the Safety, Pharmacodynamics, and Clinical Effects of WVE-120102 in Patients with Huntington's Disease

Summary

EudraCT number	2019-002178-30
Trial protocol	PL DK FR DE
Global end of trial date	03 May 2021

Results information

Result version number	v1 (current)
This version publication date	04 February 2022
First version publication date	04 February 2022

Trial information

Trial identification

Sponsor protocol code	WVE-HDSNP2-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04617860
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Wave Life Sciences UK Limited
Sponsor organisation address	1 Chamberlain Square CS, Birmingham, United Kingdom, B3 3AX
Public contact	Chief Medical Officer, Wave Life Sciences, +1 617-949-2900, info@wavelifesci.com
Scientific contact	Chief Medical Officer, Wave Life Sciences, +1 617-949-2900, info@wavelifesci.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	03 May 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 May 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of long-term exposure to WVE-120102 in patients with early manifest Huntington's disease (HD).

Protection of trial subjects:

The study was conducted according to the study protocol and standard operating procedures that meet the guidelines provided by the International Conference on Harmonisation for Good Clinical Practice in clinical studies, and any other applicable local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 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	Australia: 1
Country: Number of subjects enrolled	Canada: 21
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	Poland: 9
Worldwide total number of subjects	36
EEA total number of subjects	14

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	33
From 65 to 84 years	3

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase 1b/2a open-label extension study was conducted in adult patients with early manifest HD and who completed their final cerebrospinal fluid (CSF) collection or next visit after the final CSF collection (i.e., Day 168 or 196 depending upon dosing cohort and requirements in a given country) of the Phase 1b/2a clinical study WVE-HDSNP2-001.

Pre-assignment

Screening details:

The study consists of screening period (4 weeks), treatment period (97 weeks), and follow-up period (4 weeks). A total of 36 patients received treatment in this 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

Are arms mutually exclusive?	Yes
Arm title	4 mg WVE-120102

Arm description:

Enrolled at 4 milligram (mg) WVE-120102 dose level.

Arm type	Experimental
Investigational medicinal product name	WVE-120102
Investigational medicinal product code	WVE-120102
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

WVE-120102 4 mg was administered monthly via intrathecal dosing through Week 97.

Arm title	8 mg WVE-120102

Arm description:

Enrolled at 8 mg WVE-120102 dose level.

Arm type	Experimental
Investigational medicinal product name	WVE-120102
Investigational medicinal product code	WVE-120102
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

WVE-120102 8 mg was administered monthly via intrathecal dosing through Week 97.

Arm title	16 mg WVE-120102

Arm description:

Enrolled at 16 mg WVE-120102 dose level.

Arm type	Experimental

Investigational medicinal product name	WVE-120102
Investigational medicinal product code	WVE-120102
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

WVE-120102 16 mg was administered monthly via intrathecal dosing through Week 97.

Number of subjects in period 1	4 mg WVE-120102	8 mg WVE-120102	16 mg WVE-120102
Started	8	10	18
Dose Modified to 8 mg WVE-120102	8	1	0
Dose Modified to 16 mg WVE-120102	8	9	8
Dose Modified to 32 mg WVE-120102	2	4	11
Completed	0	0	0
Not completed	8	10	18
Physician decision	-	1	-
Consent withdrawn by subject	-	-	2
Adverse event, non-fatal	-	2	2
Termination of Study by Sponsor	8	4	13
Sponsor decision	-	3	1

Baseline characteristics

Reporting groups	
Reporting group title	4 mg WVE-120102
Reporting group description:	
Enrolled at 4 milligram (mg) WVE-120102 dose level.	
Reporting group title	8 mg WVE-120102
Reporting group description:	
Enrolled at 8 mg WVE-120102 dose level.	
Reporting group title	16 mg WVE-120102
Reporting group description:	
Enrolled at 16 mg WVE-120102 dose level.	

Reporting group values	4 mg WVE-120102	8 mg WVE-120102	16 mg WVE-120102
Number of subjects	8	10	18
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	10	16
From 65-84 years	1	0	2
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	3	6	7
Male	5	4	11
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	8	10	18
Unknown or Not Reported	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	8	10	18
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Australia	0	0	1

Canada	8	1	12
Denmark	0	5	0
Poland	0	4	5

Reporting group values	Total		
Number of subjects	36		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	33		
From 65-84 years	3		
85 years and over	0		
Gender categorical Units: Subjects			
Female	16		
Male	20		
Ethnicity Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	36		
Unknown or Not Reported	0		
Race Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	36		
More than one race	0		
Unknown or Not Reported	0		
Region of Enrollment Units: Subjects			
Australia	1		
Canada	21		
Denmark	5		
Poland	9		

End points

End points reporting groups

Reporting group title	4 mg WVE-120102
Reporting group description:	
Enrolled at 4 milligram (mg) WVE-120102 dose level.	
Reporting group title	8 mg WVE-120102
Reporting group description:	
Enrolled at 8 mg WVE-120102 dose level.	
Reporting group title	16 mg WVE-120102
Reporting group description:	
Enrolled at 16 mg WVE-120102 dose level.	
Subject analysis set title	4 mg WVE-120102
Subject analysis set type	Safety analysis
Subject analysis set description:	
Patients who received 4 mg WVE-120102 at any point in the study.	
Subject analysis set title	8 mg WVE-120102
Subject analysis set type	Safety analysis
Subject analysis set description:	
Patients who received 8 mg WVE-120102 at any point in the study.	
Subject analysis set title	16 mg WVE-120102
Subject analysis set type	Safety analysis
Subject analysis set description:	
Patients who received 16 mg WVE-120102 at any point in the study.	
Subject analysis set title	32 mg WVE-120102
Subject analysis set type	Safety analysis
Subject analysis set description:	
Patients who received 32 mg WVE-120102 at any point in the study.	

Primary: Safety: Number of Patients With Treatment-Emergent Adverse Events (TEAEs)

End point title	Safety: Number of Patients With Treatment-Emergent Adverse Events (TEAEs)[1]
End point description:	
Patients treated at more than one dose level (e.g., initial dose and after dose modification) are included in each applicable dose group. Adverse events (AEs) are counted in the dose the patient was receiving at the time of onset. A summary of serious and all other non-serious AEs, regardless of causality, is located in the reported AEs module.	
End point type	Primary
End point timeframe:	
Day 1 to Week 101/end of study	

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: Only descriptive statistical analysis was performed for the primary end point.

End point values	4 mg WVE-120102	8 mg WVE-120102	16 mg WVE-120102	32 mg WVE-120102
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	18	35	17
Units: patients	7	14	34	17

Statistical analyses

No statistical analyses for this end point

Primary: Safety: Number of Patients With a Severe TEAE

End point title	Safety: Number of Patients With a Severe TEAE[2]

End point description:

Patients treated at more than one dose level (e.g., initial dose and after dose modification) are included in each applicable dose group. AEs are counted in the dose the patient was receiving at the time of onset. A summary of serious and all other non-serious AEs, regardless of causality, is located in the reported AEs module.

End point type	Primary

End point timeframe:

Day 1 to Week 101/end of study

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: Only descriptive statistical analysis was performed for the primary end point.

End point values	4 mg WVE-120102	8 mg WVE-120102	16 mg WVE-120102	32 mg WVE-120102
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	18	35	17
Units: patients	0	0	2	5

Statistical analyses

No statistical analyses for this end point

Primary: Safety: Number of Patients With Serious TEAEs

End point title	Safety: Number of Patients With Serious TEAEs[3]

End point description:

Patients treated at more than one dose level (e.g., initial dose and after dose modification) are included in each applicable dose group. AEs are counted in the dose the patient was receiving at the time of onset. A summary of serious and all other non-serious AEs, regardless of causality, is located in the reported AEs module.

End point type	Primary

End point timeframe:

Day 1 to Week 101/end of study

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: Only descriptive statistical analysis was performed for the primary end point.

End point values	4 mg WVE-120102	8 mg WVE-120102	16 mg WVE-120102	32 mg WVE-120102
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	18	35	17
Units: patients	0	1	5	3

Statistical analyses

No statistical analyses for this end point

Primary: Safety and Tolerability: Number of Patients Who Withdraw Due to TEAEs

End point title	Safety and Tolerability: Number of Patients Who Withdraw Due to TEAEs[4]

End point description:

Patients treated at more than one dose level (e.g., initial dose and after dose modification) are included in each applicable dose group. AEs are counted in the dose the patient was receiving at the time of onset. A summary of serious and all other non-serious AEs, regardless of causality, is located in the reported AEs module.

End point type	Primary

End point timeframe:

Day 1 to Week 101/end of study

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: Only descriptive statistical analysis was performed for the primary end point.

End point values	4 mg WVE-120102	8 mg WVE-120102	16 mg WVE-120102	32 mg WVE-120102
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	18	35	17
Units: patients	0	1	3	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
First dose received (Day 1) through the Study Termination visit (maximum of 45 weeks of treatment).	
Adverse event reporting additional description:	
Safety population included all patients who received at least 1 dose of WVE-120102.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	8.2

Reporting groups	
Reporting group title	4 mg WVE-120102
Reporting group description:	
Patients who received 4 mg WVE-120102 at any point in the study.	
Reporting group title	8 mg WVE-120102
Reporting group description:	
Patients who received 8 mg WVE-120102 at any point in the study.	
Reporting group title	16 mg WVE-120102
Reporting group description:	
Patients who received 16 mg WVE-120102 at any point in the study.	
Reporting group title	32 mg WVE-120102
Reporting group description:	
Patients who received 32 mg WVE-120102 at any point in the study.	

Serious adverse events	4 mg WVE-120102	8 mg WVE-120102	16 mg WVE-120102
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	5 / 35 (14.29%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Aggression			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Meningitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	32 mg WVE-120102		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 17 (17.65%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Amnesia			

subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorder			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Aggression			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Agitation			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Confusional state			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Meningitis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningitis aseptic			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	4 mg WVE-120102	8 mg WVE-120102	16 mg WVE-120102
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)	14 / 18 (77.78%)	34 / 35 (97.14%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	6 / 35 (17.14%)
occurrences (all)	0	0	11
Gait disturbance			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Injection site erythema			
subjects affected / exposed	1 / 8 (12.50%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Injection site hypersensitivity			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 18 (0.00%)	3 / 35 (8.57%)
occurrences (all)	1	0	3
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	6 / 35 (17.14%)
occurrences (all)	0	0	9
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	1	0

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	3 / 35 (8.57%)
occurrences (all)	0	1	4
Psychiatric disorders			
Apathy			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Behaviour disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Confusional state			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	3 / 35 (8.57%)
occurrences (all)	0	0	4
Hallucination, visual			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Irritability			
subjects affected / exposed	0 / 8 (0.00%)	2 / 18 (11.11%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Paranoia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Persecutory delusion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Restlessness			

subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	3
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
CSF lymphocyte count increased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 18 (11.11%)	5 / 35 (14.29%)
occurrences (all)	0	3	6
CSF protein increased			
subjects affected / exposed	0 / 8 (0.00%)	3 / 18 (16.67%)	7 / 35 (20.00%)
occurrences (all)	0	3	9
CSF test abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
CSF white blood cell count			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Complement factor increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Dermatologic examination abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Neurological examination abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 8 (12.50%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Fall			

subjects affected / exposed	2 / 8 (25.00%)	3 / 18 (16.67%)	5 / 35 (14.29%)
occurrences (all)	2	3	5
Post procedural discomfort			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Procedural dizziness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Procedural headache			
subjects affected / exposed	1 / 8 (12.50%)	0 / 18 (0.00%)	2 / 35 (5.71%)
occurrences (all)	1	0	2
Procedural pain			
subjects affected / exposed	2 / 8 (25.00%)	0 / 18 (0.00%)	4 / 35 (11.43%)
occurrences (all)	2	0	8
Scapula fracture			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	1 / 8 (12.50%)	0 / 18 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	4 / 35 (11.43%)
occurrences (all)	0	0	7

Dysarthria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Dyskinesia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 18 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Headache			
subjects affected / exposed	2 / 8 (25.00%)	6 / 18 (33.33%)	14 / 35 (40.00%)
occurrences (all)	6	15	40
Hypotonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Migraine			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	1 / 8 (12.50%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Somnolence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	3 / 35 (8.57%)
occurrences (all)	0	0	4
Paraesthesia oral			

subjects affected / exposed	1 / 8 (12.50%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	3	0	0
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	3 / 35 (8.57%)
occurrences (all)	0	0	3
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 18 (5.56%)	6 / 35 (17.14%)
occurrences (all)	1	1	12
Muscular weakness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Myalgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Neck pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	5 / 35 (14.29%)
occurrences (all)	0	0	10
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2

Oral candidiasis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 18 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Increased appetite			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Polydipsia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 18 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	32 mg WVE-120102		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 17 (23.53%)		
occurrences (all)	5		
Gait disturbance			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Injection site erythema			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		

Injection site hypersensitivity subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 1 / 17 (5.88%) 1 1 / 17 (5.88%) 1 2 / 17 (11.76%) 2		
Reproductive system and breast disorders Breast tenderness subjects affected / exposed occurrences (all)	 0 / 17 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0		
Psychiatric disorders Apathy subjects affected / exposed occurrences (all) Behaviour disorder subjects affected / exposed occurrences (all) Confusional state subjects affected / exposed occurrences (all) Hallucination, visual subjects affected / exposed occurrences (all)	 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 5 / 17 (29.41%) 7 0 / 17 (0.00%) 0		

Insomnia				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences (all)	0			
Irritability				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Paranoia				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Persecutory delusion				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences (all)	0			
Restlessness				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences (all)	0			
Investigations				
Blood bilirubin increased				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
CSF lymphocyte count increased				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences (all)	0			
CSF protein increased				
subjects affected / exposed	4 / 17 (23.53%)			
occurrences (all)	4			
CSF test abnormal				
subjects affected / exposed	3 / 17 (17.65%)			
occurrences (all)	3			
CSF white blood cell count				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences (all)	0			
Complement factor increased				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Dermatologic examination abnormal				

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Lymphocyte count increased			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Neurological examination abnormal			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	3		
Post procedural discomfort			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Procedural dizziness			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Procedural headache			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	3		
Scapula fracture			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Skin laceration			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Nervous system disorders			

Amnesia				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Ataxia				
subjects affected / exposed	3 / 17 (17.65%)			
occurrences (all)	3			
Balance disorder				
subjects affected / exposed	2 / 17 (11.76%)			
occurrences (all)	2			
Disturbance in attention				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences (all)	0			
Dizziness				
subjects affected / exposed	3 / 17 (17.65%)			
occurrences (all)	4			
Dysarthria				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	2			
Dyskinesia				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences (all)	0			
Headache				
subjects affected / exposed	6 / 17 (35.29%)			
occurrences (all)	8			
Hypotonia				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Memory impairment				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences (all)	0			
Migraine				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	2			
Presyncope				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			

Somnolence			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	5		
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Paraesthesia oral			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 17 (29.41%)		
occurrences (all)	6		
Muscular weakness			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	4		
Myalgia			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Increased appetite			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Polydipsia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 November 2019	Included United Kingdom and Australia changes into one protocol. Clarified the schedule of assessments.
19 March 2020	Updated to move all patients to the 16 mg dose and to include language allowing patients to receive higher doses as long as they were tested in the Phase 1b/2a study.

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.

Based on the efficacy findings in this study at the time of the interim analysis, the Sponsor decided to terminate the study as the benefit/risk analysis did not warrant continued dose escalation.

Notes: