Clinical trial results:
A Multicenter, Open-label Extension Study to Evaluate the Safety, Pharmacodynamics, and Clinical Effects of WVE-120101 in Patients with Huntington's Disease

Summary

EudraCT number	2019-003637-42
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-HDSNP1-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04617847
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-120101 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: 8
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Poland: 9
Worldwide total number of subjects	27
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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	27

From 65 to 84 years	0
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-HDSNP1-001.

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 27 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-120101

Arm description:

Enrolled at 4 milligram (mg) WVE-120101 dose level.

Arm type	Experimental
Investigational medicinal product name	WVE-120101
Investigational medicinal product code	WVE-120101
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

WVE-120101 4 mg was administered monthly via intrathecal dosing through Week 97.

Arm title	16 mg WVE-120101

Arm description:

Enrolled at 16 mg WVE-120101 dose level.

Arm type	Experimental
Investigational medicinal product name	WVE-120101
Investigational medicinal product code	WVE-120101
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

WVE-120101 16 mg was administered monthly via intrathecal dosing through Week 97.

Number of subjects in period 1	4 mg WVE-120101	16 mg WVE-120101
Started	3	24
Dose Modified to 16 mg WVE-120101	3	1
Dose Modified to 32 mg WVE-120101	0	5
Completed	0	0
Not completed	3	24
Consent withdrawn by subject	1	-
Adverse event, non-fatal	-	2
Death	-	1
Termination of Study by Sponsor	2	21

Baseline characteristics

Reporting groups	
Reporting group title	4 mg WVE-120101
Reporting group description:	
Enrolled at 4 milligram (mg) WVE-120101 dose level.	
Reporting group title	16 mg WVE-120101
Reporting group description:	
Enrolled at 16 mg WVE-120101 dose level.	

Reporting group values	4 mg WVE-120101	16 mg WVE-120101	Total
Number of subjects	3	24	27
Age categorical			
Patients age at the time of enrollment in the WVE-HDSNP1-001 study is presented.			
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)	3	24	27
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	2	15	17
Male	1	9	10
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	3	24	27
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	3	24	27
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Australia	0	8	8
Canada	3	3	6
Denmark	0	2	2

France	0	2	2
Poland	0	9	9

End points

End points reporting groups

Reporting group title	4 mg WVE-120101
Reporting group description: Enrolled at 4 milligram (mg) WVE-120101 dose level.	
Reporting group title	16 mg WVE-120101
Reporting group description: Enrolled at 16 mg WVE-120101 dose level.	
Subject analysis set title	4 mg WVE-120101
Subject analysis set type	Safety analysis
Subject analysis set description: Patients who received 4 mg WVE-120101 at any point in the study.	
Subject analysis set title	16 mg WVE-120101
Subject analysis set type	Safety analysis
Subject analysis set description: Patients who received 16 mg WVE-120101 at any point in the study.	
Subject analysis set title	32 mg WVE-120101
Subject analysis set type	Safety analysis
Subject analysis set description: Patients who received 32 mg WVE-120101 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-120101	16 mg WVE-120101	32 mg WVE-120101	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	27	5	
Units: patients	2	17	2	

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-120101	16 mg WVE-120101	32 mg WVE-120101	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	27	5	
Units: patients	0	5	0	

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-120101	16 mg WVE-120101	32 mg WVE-120101	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	27	5	
Units: patients	0	3	1	

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-120101	16 mg WVE-120101	32 mg WVE-120101	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	27	5	
Units: patients	0	1	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-120101.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	8.2

Reporting groups	
Reporting group title	4 mg WVE-120101
Reporting group description:	
Patients who received 4 mg WVE-120101 at any point in the study.	
Reporting group title	16 mg WVE-120101
Reporting group description:	
Patients who received 16 mg WVE-120101 at any point in the study.	
Reporting group title	32 mg WVE-120101
Reporting group description:	
Patients who received 32 mg WVE-120101 at any point in the study.	

Serious adverse events	4 mg WVE-120101	16 mg WVE-120101	32 mg WVE-120101
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	3 / 27 (11.11%)	1 / 5 (20.00%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events	0	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung Cancer Metastatic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 27 (3.70%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Neoplasm			
subjects affected / exposed	0 / 3 (0.00%)	1 / 27 (3.70%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Injury, poisoning and procedural complications			
Head Injury			

subjects affected / exposed	0 / 3 (0.00%)	1 / 27 (3.70%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 27 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 27 (3.70%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Completed Suicide			
subjects affected / exposed	0 / 3 (0.00%)	1 / 27 (3.70%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

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

Non-serious adverse events	4 mg WVE-120101	16 mg WVE-120101	32 mg WVE-120101
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	16 / 27 (59.26%)	2 / 5 (40.00%)
Investigations			
CSF Protein Increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 27 (3.70%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
CSF white blood cell count increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 27 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 27 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	0 / 3 (0.00%)	3 / 27 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Procedural Pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 27 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	6	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 27 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	7 / 27 (25.93%)	0 / 5 (0.00%)
occurrences (all)	0	13	0
Dysarthria			
subjects affected / exposed	0 / 3 (0.00%)	2 / 27 (7.41%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	5 / 27 (18.52%)	0 / 5 (0.00%)
occurrences (all)	0	10	0
Restless legs syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 27 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 27 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	2 / 27 (7.41%)	0 / 5 (0.00%)
occurrences (all)	0	2	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 March 2020	Protocol was amended to modify dose of all patients to the 16 mg dose or higher doses, following evaluation 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: