# 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<br>Units: Subjects | | | |
| Female | 2 | 15 | 17 |
| Male | 1 | 9 | 10 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 0 |
| Not Hispanic or Latino | 3 | 24 | 27 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race<br>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<br>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: