



## Clinical trial results:

### A Multicenter, Randomized, Double-blind, Placebo-controlled, Phase 1b/2a Study of WVE-120101 Administered Intrathecally in Patients with Huntington's Disease

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2016-005095-10 |
| Trial protocol           | GB DK FR DE    |
| Global end of trial date | 11 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-HDSNP1-001 |
|-----------------------|----------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03225833 |
| 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                       | 11 May 2021 |
| Is this the analysis of the primary completion data? | No          |
| Global end of trial reached?                         | Yes         |
| Global end of trial date                             | 11 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 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                          | 05 December 2017 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Australia: 17     |
| Country: Number of subjects enrolled | Canada: 12        |
| Country: Number of subjects enrolled | Denmark: 2        |
| Country: Number of subjects enrolled | France: 4         |
| Country: Number of subjects enrolled | Germany: 4        |
| Country: Number of subjects enrolled | Poland: 19        |
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Worldwide total number of subjects   | 61                |
| EEA total number of subjects         | 29                |

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)      | 60 |
| From 65 to 84 years       | 1  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

This Phase 1b/2a placebo-controlled study was conducted in adult patients with early manifest HD who carry a targeted single nucleotide polymorphism rs362307. Following completion of this study, eligible patients were enrolled in an open-label extension study (WVE-HDSNP1-002).

### Pre-assignment

Screening details:

The study consists of prescreening period (at least 6 weeks), screening period (up to 4 weeks), single-dose period (1 day) followed by multiple-dose period (8 weeks), and follow-up period (14 weeks). A total of 61 patients received treatment in this study.

### Period 1

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

### Arms

|                              |                |
|------------------------------|----------------|
| Are arms mutually exclusive? | Yes            |
| <b>Arm title</b>             | Pooled Placebo |

Arm description:

Placebo: 0.9% Sodium Chloride.

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

Dosage and administration details:

Placebo matching with WVE-120101 was administered via intrathecal injection on Day 1 in single-dose phase followed by once every 4 weeks for a period of 8 weeks in multiple-dose phase.

|                  |                               |
|------------------|-------------------------------|
| <b>Arm title</b> | WVE-120101 (2 milligram [mg]) |
|------------------|-------------------------------|

Arm description:

WVE-120101: WVE-120101 is a stereopure antisense oligonucleotide (ASO).

|  |                                   |
|--|-----------------------------------|
| 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 2 mg administered via intrathecal injection on Day 1 in single-dose phase followed by once every 4 weeks for a period of 8 weeks in multiple-dose phase.

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | WVE-120101 (4 mg) |
|------------------|-------------------|

Arm description:

WVE-120101: WVE-120101 is a stereopure ASO.

|          |              |
|----------|--------------|
| 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 administered via intrathecal injection on Day 1 in single-dose phase followed by once every 4 weeks for a period of 8 weeks in multiple-dose phase.

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | WVE-120101 (8 mg) |
|------------------|-------------------|

Arm description:

WVE-120101: WVE-120101 is a stereopure ASO.

|  |                                   |
|--|-----------------------------------|
| 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 8 mg administered via intrathecal injection on Day 1 in single-dose phase followed by once every 4 weeks for a period of 8 weeks in multiple-dose phase.

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | WVE-120101 (16 mg) |
|------------------|--------------------|

Arm description:

WVE-120101: WVE-120101 is a stereopure ASO.

|  |                                   |
|--|-----------------------------------|
| 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 administered via intrathecal injection on Day 1 in single-dose phase followed by once every 4 weeks for a period of 8 weeks in multiple-dose phase.

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | WVE-120101 (32 mg) |
|------------------|--------------------|

Arm description:

WVE-120101: WVE-120101 is a stereopure ASO.

|  |                                   |
|--|-----------------------------------|
| 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 32 mg administered via intrathecal injection on Day 1 in single-dose phase followed by once every 4 weeks for a period of 8 weeks in multiple-dose phase.

| <b>Number of subjects in period 1</b> | Pooled Placebo   | WVE-120101 (2 milligram [mg]) | WVE-120101 (4 mg) |
|---------------------------------------|------------------|-------------------------------|-------------------|
| Started                               | 16               | 9                             | 9                 |
| Single Dose Period Only               | 1 <sup>[1]</sup> | 1 <sup>[2]</sup>              | 2 <sup>[3]</sup>  |
| Multiple Dose Period Only             | 0 <sup>[4]</sup> | 0 <sup>[5]</sup>              | 0 <sup>[6]</sup>  |
| Single Dose and Multiple Dose Periods | 15               | 8                             | 7                 |
| Completed                             | 11               | 8                             | 7                 |
| Not completed                         | 5                | 1                             | 2                 |
| Consent withdrawn by subject          | 1                | -                             | -                 |
| Adverse event, non-fatal              | -                | 1                             | 2                 |
| Sponsor Decision                      | -                | -                             | -                 |
| Termination of Study by Sponsor       | 4                | -                             | -                 |

| <b>Number of subjects in period 1</b> | WVE-120101 (8 mg) | WVE-120101 (16 mg) | WVE-120101 (32 mg) |
|---------------------------------------|-------------------|--------------------|--------------------|
| Started                               | 9                 | 8                  | 10                 |
| Single Dose Period Only               | 0 <sup>[7]</sup>  | 0 <sup>[8]</sup>   | 4                  |
| Multiple Dose Period Only             | 0 <sup>[9]</sup>  | 0 <sup>[10]</sup>  | 1                  |
| Single Dose and Multiple Dose Periods | 9                 | 8                  | 5                  |
| Completed                             | 9                 | 7                  | 0                  |
| Not completed                         | 0                 | 1                  | 10                 |
| Consent withdrawn by subject          | -                 | 1                  | -                  |
| Adverse event, non-fatal              | -                 | -                  | 2                  |
| Sponsor Decision                      | -                 | -                  | 1                  |
| Termination of Study by Sponsor       | -                 | -                  | 7                  |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.

[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.

## Baseline characteristics

| <b>Reporting groups</b>   |                               |
|---|-------------------------------|
| Reporting group title   | Pooled Placebo                |
| Reporting group description:<br>Placebo: 0.9% Sodium Chloride.  |                               |
| Reporting group title   | WVE-120101 (2 milligram [mg]) |
| Reporting group description:<br>WVE-120101: WVE-120101 is a stereopure antisense oligonucleotide (ASO). |                               |
| Reporting group title   | WVE-120101 (4 mg)             |
| Reporting group description:<br>WVE-120101: WVE-120101 is a stereopure ASO.                             |                               |
| Reporting group title   | WVE-120101 (8 mg)             |
| Reporting group description:<br>WVE-120101: WVE-120101 is a stereopure ASO.                             |                               |
| Reporting group title   | WVE-120101 (16 mg)            |
| Reporting group description:<br>WVE-120101: WVE-120101 is a stereopure ASO.                             |                               |
| Reporting group title   | WVE-120101 (32 mg)            |
| Reporting group description:<br>WVE-120101: WVE-120101 is a stereopure ASO.                             |                               |

| <b>Reporting group values</b>                      | Pooled Placebo | WVE-120101 (2 milligram [mg]) | WVE-120101 (4 mg) |
|--|----------------|-------------------------------|-------------------|
| Number of subjects                                 | 16             | 9                             | 9                 |
| Age categorical<br>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)                               | 15             | 9                             | 9                 |
| From 65-84 years                                   | 1              | 0                             | 0                 |
| 85 years and over                                  | 0              | 0                             | 0                 |
| Gender categorical<br>Units: Subjects              |                |                               |                   |
| Female   | 7              | 3                             | 5                 |
| Male   | 9              | 6                             | 4                 |
| Ethnicity<br>Units: Subjects                       |                |                               |                   |
| Hispanic or Latino                                 | 0              | 0                             | 0                 |
| Not Hispanic or Latino                             | 16             | 9                             | 9                 |
| 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                                     | 16       | 9       | 9       |
| More than one race                        | 0        | 0       | 0       |
| Unknown or Not Reported                   | 0        | 0       | 0       |
| <b>Region of Enrollment</b>               |          |         |         |
| Units: Subjects                           |          |         |         |
| Australia                                 | 4        | 0       | 0       |
| Canada                                    | 4        | 2       | 2       |
| Denmark                                   | 0        | 0       | 0       |
| France                                    | 1        | 0       | 0       |
| Germany                                   | 2        | 0       | 0       |
| Poland                                    | 4        | 7       | 5       |
| United Kingdom                            | 1        | 0       | 2       |
| <b>Diagnosis Stage</b>                    |          |         |         |
| Units: Subjects                           |          |         |         |
| Stage 1                                   | 9        | 7       | 3       |
| Stage 2                                   | 7        | 2       | 6       |
| <b>Time since initial diagnosis</b>       |          |         |         |
| Units: years                              |          |         |         |
| arithmetic mean                           | 7        | 4.9     | 3.4     |
| standard deviation                        | ± 6.93   | ± 4.28  | ± 6.37  |
| <b>Age at Disease Onset</b>               |          |         |         |
| Units: years                              |          |         |         |
| arithmetic mean                           | 40.75    | 37.33   | 42.89   |
| standard deviation                        | ± 11.079 | ± 7.826 | ± 9.280 |

| <b>Reporting group values</b>                      | WVE-120101 (8 mg) | WVE-120101 (16 mg) | WVE-120101 (32 mg) |
|--|-------------------|--------------------|--------------------|
| Number of subjects                                 | 9                 | 8                  | 10                 |
| <b>Age categorical</b>                             |                   |                    |                    |
| 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)                               | 9                 | 8                  | 10                 |
| From 65-84 years                                   | 0                 | 0                  | 0                  |
| 85 years and over                                  | 0                 | 0                  | 0                  |
| <b>Gender categorical</b>                          |                   |                    |                    |
| Units: Subjects                                    |                   |                    |                    |
| Female   | 6                 | 1                  | 7                  |
| Male   | 3                 | 7                  | 3                  |
| <b>Ethnicity</b>                                   |                   |                    |                    |
| Units: Subjects                                    |                   |                    |                    |
| Hispanic or Latino                                 | 0                 | 0                  | 0                  |
| Not Hispanic or Latino                             | 9                 | 8                  | 10                 |

|   |         |          |          |
|---|---------|----------|----------|
| 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                                     | 9       | 8        | 10       |
| More than one race                        | 0       | 0        | 0        |
| Unknown or Not Reported                   | 0       | 0        | 0        |
| Region of Enrollment                      |         |          |          |
| Units: Subjects                           |         |          |          |
| Australia                                 | 6       | 3        | 4        |
| Canada                                    | 1       | 0        | 3        |
| Denmark                                   | 1       | 1        | 0        |
| France                                    | 0       | 1        | 2        |
| Germany                                   | 0       | 1        | 1        |
| Poland                                    | 1       | 2        | 0        |
| United Kingdom                            | 0       | 0        | 0        |
| Diagnosis Stage                           |         |          |          |
| Units: Subjects                           |         |          |          |
| Stage 1                                   | 3       | 4        | 7        |
| Stage 2                                   | 6       | 4        | 3        |
| Time since initial diagnosis              |         |          |          |
| Units: years                              |         |          |          |
| arithmetic mean                           | 3.2     | 6.6      | 8.7      |
| standard deviation                        | ± 3.03  | ± 6.09   | ± 7.26   |
| Age at Disease Onset                      |         |          |          |
| Units: years                              |         |          |          |
| arithmetic mean                           | 46.11   | 44.88    | 44.60    |
| standard deviation                        | ± 6.254 | ± 12.495 | ± 10.865 |

|  |       |  |  |
|--|-------|--|--|
| <b>Reporting group values</b>                      | Total |  |  |
| Number of subjects                                 | 61    |  |  |
| 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)                               | 60    |  |  |
| From 65-84 years                                   | 1     |  |  |
| 85 years and over                                  | 0     |  |  |
| Gender categorical                                 |       |  |  |
| Units: Subjects                                    |       |  |  |
| Female   | 29    |  |  |
| Male   | 32    |  |  |

|   |    |  |  |
|---|----|--|--|
| Ethnicity                                 |    |  |  |
| Units: Subjects                           |    |  |  |
| Hispanic or Latino                        | 0  |  |  |
| Not Hispanic or Latino                    | 61 |  |  |
| 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                                     | 61 |  |  |
| More than one race                        | 0  |  |  |
| Unknown or Not Reported                   | 0  |  |  |
| Region of Enrollment                      |    |  |  |
| Units: Subjects                           |    |  |  |
| Australia                                 | 17 |  |  |
| Canada                                    | 12 |  |  |
| Denmark                                   | 2  |  |  |
| France                                    | 4  |  |  |
| Germany                                   | 4  |  |  |
| Poland                                    | 19 |  |  |
| United Kingdom                            | 3  |  |  |
| Diagnosis Stage                           |    |  |  |
| Units: Subjects                           |    |  |  |
| Stage 1                                   | 33 |  |  |
| Stage 2                                   | 28 |  |  |
| Time since initial diagnosis              |    |  |  |
| Units: years                              |    |  |  |
| arithmetic mean                           |    |  |  |
| standard deviation                        | -  |  |  |
| Age at Disease Onset                      |    |  |  |
| Units: years                              |    |  |  |
| arithmetic mean                           |    |  |  |
| standard deviation                        | -  |  |  |

## End points

### End points reporting groups

|   |                               |
|---|-------------------------------|
| Reporting group title   | Pooled Placebo                |
| Reporting group description:<br>Placebo: 0.9% Sodium Chloride.  |                               |
| Reporting group title   | WVE-120101 (2 milligram [mg]) |
| Reporting group description:<br>WVE-120101: WVE-120101 is a stereopure antisense oligonucleotide (ASO). |                               |
| Reporting group title   | WVE-120101 (4 mg)             |
| Reporting group description:<br>WVE-120101: WVE-120101 is a stereopure ASO.                             |                               |
| Reporting group title   | WVE-120101 (8 mg)             |
| Reporting group description:<br>WVE-120101: WVE-120101 is a stereopure ASO.                             |                               |
| Reporting group title   | WVE-120101 (16 mg)            |
| Reporting group description:<br>WVE-120101: WVE-120101 is a stereopure ASO.                             |                               |
| Reporting group title   | WVE-120101 (32 mg)            |
| Reporting group description:<br>WVE-120101: WVE-120101 is a stereopure ASO.                             |                               |

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

|  |  |
|--|--|
| End point title  | Safety: Number of Patients With Treatment-emergent Adverse Events (TEAEs) <sup>[1]</sup> |
| End point description:<br>All TEAEs reported or observed during the study, including TEAEs resulting from concurrent illnesses, reactions to concurrent medications, or progression of disease states. Safety population included all patients who received at least 1 dose of WVE-120101 or placebo. A summary of serious and all other non-serious adverse events (AEs), regardless of causality, is located in the reported AEs module. |  |
| End point type   | Primary  |
| End point timeframe:<br>Day 1 to end of study (up to Day 182 [32 mg cohort]/ Day 210 [all other cohorts])  |  |

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            | Pooled Placebo  | WVE-120101<br>(2 milligram<br>[mg]) | WVE-120101<br>(4 mg) | WVE-120101<br>(8 mg) |
|-----------------------------|-----------------|-------------------------------------|----------------------|----------------------|
| Subject group type          | Reporting group | Reporting group                     | Reporting group      | Reporting group      |
| Number of subjects analysed | 16              | 9                                   | 9                    | 9                    |
| Units: patients             | 12              | 8                                   | 8                    | 9                    |

| End point values | WVE-120101<br>(16 mg) | WVE-120101<br>(32 mg) |  |  |
|------------------|-----------------------|-----------------------|--|--|
|                  |                       |                       |  |  |

|                             |                 |                 |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 8               | 10              |  |  |
| Units: patients             | 7               | 9               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Safety: Number of Patients With Severe TEAEs

|                 |   |
|-----------------|---|
| End point title | Safety: Number of Patients With Severe TEAEs <sup>[2]</sup> |
|-----------------|---|

End point description:

Severity was evaluated using the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0. Safety population included all patients who received at least 1 dose of WVE-120101 or placebo. 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 end of study (up to Day 182 [32 mg cohort]/ Day 210 [all other cohorts])

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            | Pooled Placebo  | WVE-120101<br>(2 milligram<br>[mg]) | WVE-120101<br>(4 mg) | WVE-120101<br>(8 mg) |
|-----------------------------|-----------------|-------------------------------------|----------------------|----------------------|
| Subject group type          | Reporting group | Reporting group                     | Reporting group      | Reporting group      |
| Number of subjects analysed | 16              | 9                                   | 9                    | 9                    |
| Units: patients             | 1               | 2                                   | 1                    | 1                    |

| End point values            | WVE-120101<br>(16 mg) | WVE-120101<br>(32 mg) |  |  |
|-----------------------------|-----------------------|-----------------------|--|--|
| Subject group type          | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed | 8                     | 10                    |  |  |
| Units: patients             | 0                     | 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 <sup>[3]</sup> |
|-----------------|--|

End point description:

A serious TEAE is defined as any event that results in death, is immediately life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect not present at prescreening. Safety population included all patients who received at least 1 dose of WVE-120101 or placebo. 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 end of study (up to Day 182 [32 mg cohort]/ Day 210 [all other cohorts])

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            | Pooled Placebo  | WVE-120101<br>(2 milligram<br>[mg]) | WVE-120101<br>(4 mg) | WVE-120101<br>(8 mg) |
|-----------------------------|-----------------|-------------------------------------|----------------------|----------------------|
| Subject group type          | Reporting group | Reporting group                     | Reporting group      | Reporting group      |
| Number of subjects analysed | 16              | 9                                   | 9                    | 9                    |
| Units: patients             | 0               | 2                                   | 1                    | 0                    |

| End point values            | WVE-120101<br>(16 mg) | WVE-120101<br>(32 mg) |  |  |
|-----------------------------|-----------------------|-----------------------|--|--|
| Subject group type          | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed | 8                     | 10                    |  |  |
| Units: patients             | 0                     | 4                     |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Safety and Tolerability: Number of Patients Who Withdraw From the Study Due to TEAEs

|                 |   |
|-----------------|---|
| End point title | Safety and Tolerability: Number of Patients Who Withdraw From the Study Due to TEAEs <sup>[4]</sup> |
|-----------------|---|

End point description:

Patients withdraw from the study when serious or intolerable AE that in the Investigator's opinion was reported. Safety population included all patients who received at least 1 dose of WVE-120101 or placebo. 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 end of study (up to Day 182 [32 mg cohort]/ Day 210 [all other cohorts])

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            | Pooled Placebo  | WVE-120101<br>(2 milligram<br>[mg]) | WVE-120101<br>(4 mg) | WVE-120101<br>(8 mg) |
|-----------------------------|-----------------|-------------------------------------|----------------------|----------------------|
| Subject group type          | Reporting group | Reporting group                     | Reporting group      | Reporting group      |
| Number of subjects analysed | 16              | 9                                   | 9                    | 9                    |
| Units: patients             | 0               | 1                                   | 2                    | 0                    |

|                             |                       |                       |  |  |
|-----------------------------|-----------------------|-----------------------|--|--|
| <b>End point values</b>     | WVE-120101<br>(16 mg) | WVE-120101<br>(32 mg) |  |  |
| Subject group type          | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed | 8                     | 10                    |  |  |
| Units: patients             | 0                     | 2                     |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics (PK): Maximum Observed Concentration (Cmax)

|                 |   |
|-----------------|---|
| End point title | Pharmacokinetics (PK): Maximum Observed Concentration (Cmax) <sup>[5]</sup> |
|-----------------|---|

End point description:

Cmax of WVE-120101 in plasma. The PK population included all treated patients in the safety population with at least 1 post-dose plasma or cerebrospinal fluid (CSF) WVE-120101 concentration measurement. Here, n= number of patients analyzed at specific timepoint and '99999'= not applicable as no patient was analyzed.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 up to Day 140 (32 mg cohort) or Day 196 (all other cohorts)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only reporting groups in which patients received WVE-120101 were evaluated for this PK end point.

|  |                                     |                      |                      |                       |
|--|-------------------------------------|----------------------|----------------------|-----------------------|
| <b>End point values</b>                | WVE-120101<br>(2 milligram<br>[mg]) | WVE-120101<br>(4 mg) | WVE-120101<br>(8 mg) | WVE-120101<br>(16 mg) |
| Subject group type                     | Reporting group                     | Reporting group      | Reporting group      | Reporting group       |
| Number of subjects analysed            | 9                                   | 9                    | 9                    | 8                     |
| Units: nanogram per milliliter (ng/mL) |                                     |                      |                      |                       |
| arithmetic mean (standard deviation)   |                                     |                      |                      |                       |
| Day 1 (n= 9, 9, 9, 8, 10)              | 7.70 (± 7.901)                      | 23.54 (± 18.139)     | 32.82 (± 22.964)     | 184.48 (± 209.470)    |
| Day 112 (n= 9, 4, 0, 0, 0)             | 13.296 (± 6.057)                    | 14.27 (± 12.574)     | 99999 (± 99999)      | 99999 (± 99999)       |

|  |                       |  |  |  |
|--|-----------------------|--|--|--|
| <b>End point values</b>                | WVE-120101<br>(32 mg) |  |  |  |
| Subject group type                     | Reporting group       |  |  |  |
| Number of subjects analysed            | 10                    |  |  |  |
| Units: nanogram per milliliter (ng/mL) |                       |  |  |  |
| arithmetic mean (standard deviation)   |                       |  |  |  |
| Day 1 (n= 9, 9, 9, 8, 10)              | 229.01 (± 168.330)    |  |  |  |

|                            |                 |  |  |  |
|----------------------------|-----------------|--|--|--|
| Day 112 (n= 9, 4, 0, 0, 0) | 99999 (± 99999) |  |  |  |
|----------------------------|-----------------|--|--|--|

## Statistical analyses

No statistical analyses for this end point

### Secondary: PK: Time of Occurrence of Cmax (Tmax)

|                 |  |
|-----------------|--|
| End point title | PK: Time of Occurrence of Cmax (Tmax) <sup>[6]</sup> |
|-----------------|--|

End point description:

Tmax of WVE-120101 in plasma. The PK population included all treated patients in the safety population with at least 1 post-dose plasma or CSF WVE-120101 concentration measurement. Here, n= number of patients analyzed at specific timepoint and '99999'= not applicable as no patient was analyzed.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 up to Day 140 (32 mg cohort) or Day 196 (all other cohorts)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only reporting groups in which patients received WVE-120101 were evaluated for this PK end point.

| End point values                     | WVE-120101<br>(2 milligram<br>[mg]) | WVE-120101<br>(4 mg) | WVE-120101<br>(8 mg) | WVE-120101<br>(16 mg) |
|--------------------------------------|-------------------------------------|----------------------|----------------------|-----------------------|
| Subject group type                   | Reporting group                     | Reporting group      | Reporting group      | Reporting group       |
| Number of subjects analysed          | 9                                   | 9                    | 9                    | 8                     |
| Units: hour                          |                                     |                      |                      |                       |
| arithmetic mean (standard deviation) |                                     |                      |                      |                       |
| Day 1 (n= 9, 9, 9, 8, 10)            | 1.34 (± 1.103)                      | 1.58 (± 1.081)       | 2.66 (± 1.391)       | 2.71 (± 3.068)        |
| Day 112 (n= 9, 4, 0, 0, 0)           | 1.99 (± 0.934)                      | 2.23 (± 1.175)       | 99999 (± 99999)      | 99999 (± 99999)       |

| End point values                     | WVE-120101<br>(32 mg) |  |  |  |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type                   | Reporting group       |  |  |  |
| Number of subjects analysed          | 10                    |  |  |  |
| Units: hour                          |                       |  |  |  |
| arithmetic mean (standard deviation) |                       |  |  |  |
| Day 1 (n= 9, 9, 9, 8, 10)            | 4.61 (± 7.054)        |  |  |  |
| Day 112 (n= 9, 4, 0, 0, 0)           | 99999 (± 99999)       |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: PK: Area Under the Plasma Concentration-time Curve (AUClast)

End point title | PK: Area Under the Plasma Concentration-time Curve

End point description:

AUClast from time 0 to the last quantifiable concentration of WVE-120101 in plasma. The PK population included all treated patients in the safety population with at least 1 post-dose plasma or CSF WVE-120101 concentration measurement. Here, n= number of patients analyzed at specific timepoint and '99999'= not applicable as no patient was analyzed.

End point type | Secondary

End point timeframe:

Day 1 up to Day 140 (32 mg cohort) or Day 196 (all other cohorts)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only reporting groups in which patients received WVE-120101 were evaluated for this PK end point.

| End point values                     | WVE-120101<br>(2 milligram<br>[mg]) | WVE-120101<br>(4 mg) | WVE-120101<br>(8 mg) | WVE-120101<br>(16 mg)  |
|--------------------------------------|-------------------------------------|----------------------|----------------------|------------------------|
| Subject group type                   | Reporting group                     | Reporting group      | Reporting group      | Reporting group        |
| Number of subjects analysed          | 9                                   | 9                    | 9                    | 8                      |
| Units: hour*ng/mL                    |                                     |                      |                      |                        |
| arithmetic mean (standard deviation) |                                     |                      |                      |                        |
| Day 1 (n= 5, 8, 8, 8, 9)             | 35.20 (±<br>16.037)                 | 90.77 (±<br>50.672)  | 255.14 (±<br>98.342) | 1133.74 (±<br>551.997) |
| Day 112 (n= 8, 3, 0, 0, 0)           | 36.19 (±<br>20.135)                 | 49.54 (±<br>34.735)  | 99999 (±<br>99999)   | 99999 (±<br>99999)     |

| End point values                     | WVE-120101<br>(32 mg)   |  |  |  |
|--------------------------------------|-------------------------|--|--|--|
| Subject group type                   | Reporting group         |  |  |  |
| Number of subjects analysed          | 10                      |  |  |  |
| Units: hour*ng/mL                    |                         |  |  |  |
| arithmetic mean (standard deviation) |                         |  |  |  |
| Day 1 (n= 5, 8, 8, 8, 9)             | 1968.31 (±<br>1188.173) |  |  |  |
| Day 112 (n= 8, 3, 0, 0, 0)           | 99999 (±<br>99999)      |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: PK: Terminal Elimination Rate Constant

End point title | PK: Terminal Elimination Rate Constant<sup>[8]</sup>

End point description:

Elimination rate of WVE-120101 from plasma (t<sub>1/2</sub>). The PK population included all treated patients in the safety population with at least 1 post-dose plasma or CSF WVE-120101 concentration measurement.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 up to Day 140 (32 mg cohort) or Day 196 (all other cohorts)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only reporting groups in which patients received WVE-120101 were evaluated for this PK end point.

| End point values              | WVE-120101<br>(2 milligram<br>[mg]) | WVE-120101<br>(4 mg) | WVE-120101<br>(8 mg)  | WVE-120101<br>(16 mg)  |
|-------------------------------|-------------------------------------|----------------------|-----------------------|------------------------|
| Subject group type            | Reporting group                     | Reporting group      | Reporting group       | Reporting group        |
| Number of subjects analysed   | 0 <sup>[9]</sup>                    | 0 <sup>[10]</sup>    | 9                     | 8                      |
| Units: hour                   |                                     |                      |                       |                        |
| median (full range (min-max)) | ( to )                              | ( to )               | 8.12 (7.1 to<br>40.0) | 12.30 (6.9 to<br>25.5) |

Notes:

[9] - No patients were analyzed for this endpoint.

[10] - No patients were analyzed for this endpoint.

| End point values              | WVE-120101<br>(32 mg)  |  |  |  |
|-------------------------------|------------------------|--|--|--|
| Subject group type            | Reporting group        |  |  |  |
| Number of subjects analysed   | 10                     |  |  |  |
| Units: hour                   |                        |  |  |  |
| median (full range (min-max)) | 14.38 (5.5 to<br>46.9) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacodynamics: Percent Change From Baseline in the Concentration of Mutant Huntingtin (mHTT) Protein at the Last Measured Observation

|                 |  |
|-----------------|--|
| End point title | Pharmacodynamics: Percent Change From Baseline in the Concentration of Mutant Huntingtin (mHTT) Protein at the Last Measured Observation |
|-----------------|--|

End point description:

Percent change from baseline in concentration of mHTT protein in CSF was determined. Safety population included all patients who received at least 1 dose of WVE-120101 or placebo.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and last observation (up to Day 140 [32 mg cohort] or Day 196 [all other cohorts])

| <b>End point values</b>               | Pooled Placebo            | WVE-120101<br>(2 milligram<br>[mg]) | WVE-120101<br>(4 mg)       | WVE-120101<br>(8 mg)       |
|---------------------------------------|---------------------------|-------------------------------------|----------------------------|----------------------------|
| Subject group type                    | Reporting group           | Reporting group                     | Reporting group            | Reporting group            |
| Number of subjects analysed           | 16                        | 9                                   | 9                          | 9                          |
| Units: percent change                 |                           |                                     |                            |                            |
| median (inter-quartile range (Q1-Q3)) | -6.62 (-16.76<br>to 7.73) | -5.20 (-10.94<br>to 0.15)           | -12.33 (-19.81<br>to 9.63) | -8.58 (-11.92<br>to -1.79) |

| <b>End point values</b>               | WVE-120101<br>(16 mg)      | WVE-120101<br>(32 mg)      |  |  |
|---------------------------------------|----------------------------|----------------------------|--|--|
| Subject group type                    | Reporting group            | Reporting group            |  |  |
| Number of subjects analysed           | 8                          | 10                         |  |  |
| Units: percent change                 |                            |                            |  |  |
| median (inter-quartile range (Q1-Q3)) | -11.73 (-20.44<br>to 3.37) | -9.13 (-37.51<br>to 15.29) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Clinical Effects: Percent Change From Baseline in the Total Functional Capacity (TFC) at the Last Measured Observation

|                 |  |
|-----------------|--|
| End point title | Clinical Effects: Percent Change From Baseline in the Total Functional Capacity (TFC) at the Last Measured Observation |
|-----------------|--|

End point description:

Percent change from baseline in the TFC, administered as part of the Unified Huntington's Disease Rating Scale was determined. Safety population included all patients who received at least 1 dose of WVE-120101 or placebo.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and last observation (up to Day 140 [32 mg cohort] or Day 196 [all other cohorts])

| <b>End point values</b>               | Pooled Placebo          | WVE-120101<br>(2 milligram<br>[mg]) | WVE-120101<br>(4 mg)     | WVE-120101<br>(8 mg)     |
|---------------------------------------|-------------------------|-------------------------------------|--------------------------|--------------------------|
| Subject group type                    | Reporting group         | Reporting group                     | Reporting group          | Reporting group          |
| Number of subjects analysed           | 16                      | 9                                   | 9                        | 9                        |
| Units: percent change                 |                         |                                     |                          |                          |
| median (inter-quartile range (Q1-Q3)) | 0.00 (-9.09 to<br>0.00) | 0.00 (-4.17 to<br>9.09)             | 0.00 (-7.69 to<br>11.11) | 0.00 (-20.00 to<br>0.00) |

| <b>End point values</b> | WVE-120101<br>(16 mg) | WVE-120101<br>(32 mg) |  |  |
|-------------------------|-----------------------|-----------------------|--|--|
|                         |                       |                       |  |  |

|                                       |                       |                     |  |  |
|---------------------------------------|-----------------------|---------------------|--|--|
| Subject group type                    | Reporting group       | Reporting group     |  |  |
| Number of subjects analysed           | 8                     | 10                  |  |  |
| Units: percent change                 |                       |                     |  |  |
| median (inter-quartile range (Q1-Q3)) | 4.17 (-3.85 to 10.42) | 0.00 (0.00 to 0.00) |  |  |

## Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 1 to end of study (Day 182 [32 mg cohort in all regions except Canada] or Day 196 [32 mg cohort in Canada] or Day 210 [all other cohorts]).

Adverse event reporting additional description:

Safety population included all patients who received at least 1 dose of WVE-120101 or placebo.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |     |
|--------------------|-----|
| Dictionary version | 8.2 |
|--------------------|-----|

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | Pooled Placebo |
|-----------------------|----------------|

Reporting group description:

Placebo: 0.9% Sodium Chloride.

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | WVE-120101 (2 mg) |
|-----------------------|-------------------|

Reporting group description:

WVE-120101: WVE-120101 is a stereopure ASO.

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | WVE-120101 (4 mg) |
|-----------------------|-------------------|

Reporting group description:

WVE-120101: WVE-120101 is a stereopure ASO.

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | WVE-120101 (8 mg) |
|-----------------------|-------------------|

Reporting group description:

WVE-120101: WVE-120101 is a stereopure ASO.

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | WVE-120101 (16 mg) |
|-----------------------|--------------------|

Reporting group description:

WVE-120101: WVE-120101 is a stereopure ASO.

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | WVE-120101 (32 mg) |
|-----------------------|--------------------|

Reporting group description:

WVE-120101: WVE-120101 is a stereopure ASO.

| <b>Serious adverse events</b>                                       | Pooled Placebo | WVE-120101 (2 mg) | WVE-120101 (4 mg) |
|---|----------------|-------------------|-------------------|
| Total subjects affected by serious adverse events                   |                |                   |                   |
| subjects affected / exposed   | 0 / 16 (0.00%) | 2 / 9 (22.22%)    | 1 / 9 (11.11%)    |
| number of deaths (all causes)                                       | 0              | 0                 | 0                 |
| number of deaths resulting from adverse events                      | 0              | 0                 | 0                 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                   |                   |
| Adenocarcinoma of colon   |                |                   |                   |
| subjects affected / exposed   | 0 / 16 (0.00%) | 1 / 9 (11.11%)    | 0 / 9 (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             |
| Injury, poisoning and procedural complications                      |                |                   |                   |

|  |                |               |                |
|--|----------------|---------------|----------------|
| Ankle fracture                                       |                |               |                |
| subjects affected / exposed                          | 0 / 16 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (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          |
| Fall   |                |               |                |
| subjects affected / exposed                          | 0 / 16 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (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          |
| Skull Fracture                                       |                |               |                |
| subjects affected / exposed                          | 0 / 16 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0          |
| Subdural haematoma                                   |                |               |                |
| subjects affected / exposed                          | 0 / 16 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0          |
| Nervous system disorders                             |                |               |                |
| Ataxia   |                |               |                |
| subjects affected / exposed                          | 0 / 16 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (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          |
| Dysarthria   |                |               |                |
| subjects affected / exposed                          | 0 / 16 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (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 |                |               |                |
| Gait disturbance                                     |                |               |                |
| subjects affected / exposed                          | 0 / 16 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (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          |
| Psychiatric disorders                                |                |               |                |
| Aggression   |                |               |                |

|  |                |                |               |
|--|----------------|----------------|---------------|
| subjects affected / exposed                            | 0 / 16 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (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         |
| <b>Agitation</b>                                       |                |                |               |
| subjects affected / exposed                            | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 0 / 9 (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         |
| <b>Disorientation</b>                                  |                |                |               |
| subjects affected / exposed                            | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 0 / 9 (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         |
| <b>Musculoskeletal and connective tissue disorders</b> |                |                |               |
| <b>Muscular weakness</b>                               |                |                |               |
| subjects affected / exposed                            | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 0 / 9 (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         |

| <b>Serious adverse events</b>  | WVE-120101 (8 mg) | WVE-120101 (16 mg) | WVE-120101 (32 mg) |
|--|-------------------|--------------------|--------------------|
| <b>Total subjects affected by serious adverse events</b>                   |                   |                    |                    |
| subjects affected / exposed  | 0 / 9 (0.00%)     | 0 / 8 (0.00%)      | 4 / 10 (40.00%)    |
| number of deaths (all causes)  | 0                 | 0                  | 0                  |
| number of deaths resulting from adverse events                             | 0                 | 0                  | 0                  |
| <b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b> |                   |                    |                    |
| <b>Adenocarcinoma of colon</b>   |                   |                    |                    |
| subjects affected / exposed  | 0 / 9 (0.00%)     | 0 / 8 (0.00%)      | 0 / 10 (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              |
| <b>Injury, poisoning and procedural complications</b>                      |                   |                    |                    |
| <b>Ankle fracture</b>  |                   |                    |                    |
| subjects affected / exposed  | 0 / 9 (0.00%)     | 0 / 8 (0.00%)      | 1 / 10 (10.00%)    |
| occurrences causally related to treatment / all                            | 0 / 0             | 0 / 0              | 0 / 1              |
| deaths causally related to treatment / all                                 | 0 / 0             | 0 / 0              | 0 / 0              |
| <b>Fall</b>  |                   |                    |                    |

|   |               |               |                 |
|---|---------------|---------------|-----------------|
| subjects affected / exposed                                 | 0 / 9 (0.00%) | 0 / 8 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all             | 0 / 0         | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all                  | 0 / 0         | 0 / 0         | 0 / 0           |
| <b>Skull Fracture</b>                                       |               |               |                 |
| subjects affected / exposed                                 | 0 / 9 (0.00%) | 0 / 8 (0.00%) | 0 / 10 (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           |
| <b>Subdural haematoma</b>                                   |               |               |                 |
| subjects affected / exposed                                 | 0 / 9 (0.00%) | 0 / 8 (0.00%) | 0 / 10 (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           |
| <b>Nervous system disorders</b>                             |               |               |                 |
| <b>Ataxia</b>   |               |               |                 |
| subjects affected / exposed                                 | 0 / 9 (0.00%) | 0 / 8 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all             | 0 / 0         | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all                  | 0 / 0         | 0 / 0         | 0 / 0           |
| <b>Dysarthria</b>   |               |               |                 |
| subjects affected / exposed                                 | 0 / 9 (0.00%) | 0 / 8 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all             | 0 / 0         | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all                  | 0 / 0         | 0 / 0         | 0 / 0           |
| <b>General disorders and administration site conditions</b> |               |               |                 |
| <b>Gait disturbance</b>                                     |               |               |                 |
| subjects affected / exposed                                 | 0 / 9 (0.00%) | 0 / 8 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all             | 0 / 0         | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all                  | 0 / 0         | 0 / 0         | 0 / 0           |
| <b>Psychiatric disorders</b>                                |               |               |                 |
| <b>Aggression</b>   |               |               |                 |
| subjects affected / exposed                                 | 0 / 9 (0.00%) | 0 / 8 (0.00%) | 0 / 10 (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           |
| <b>Agitation</b>  |               |               |                 |
| subjects affected / exposed                                 | 0 / 9 (0.00%) | 0 / 8 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all             | 0 / 0         | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all                  | 0 / 0         | 0 / 0         | 0 / 0           |

|   |               |               |                 |
|---|---------------|---------------|-----------------|
| Disorientation                                  |               |               |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 8 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0           |
| Musculoskeletal and connective tissue disorders |               |               |                 |
| Muscular weakness                               |               |               |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 8 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0           |

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

| <b>Non-serious adverse events</b>                     | Pooled Placebo   | WVE-120101 (2 mg) | WVE-120101 (4 mg) |
|---|------------------|-------------------|-------------------|
| Total subjects affected by non-serious adverse events |                  |                   |                   |
| subjects affected / exposed                           | 12 / 16 (75.00%) | 8 / 9 (88.89%)    | 8 / 9 (88.89%)    |
| Vascular disorders                                    |                  |                   |                   |
| Flushing  |                  |                   |                   |
| subjects affected / exposed                           | 1 / 16 (6.25%)   | 0 / 9 (0.00%)     | 0 / 9 (0.00%)     |
| occurrences (all)                                     | 1                | 0                 | 0                 |
| Hot flush   |                  |                   |                   |
| subjects affected / exposed                           | 0 / 16 (0.00%)   | 0 / 9 (0.00%)     | 0 / 9 (0.00%)     |
| occurrences (all)                                     | 0                | 0                 | 0                 |
| Hypertension  |                  |                   |                   |
| subjects affected / exposed                           | 1 / 16 (6.25%)   | 1 / 9 (11.11%)    | 0 / 9 (0.00%)     |
| occurrences (all)                                     | 1                | 1                 | 0                 |
| Hypotension   |                  |                   |                   |
| subjects affected / exposed                           | 0 / 16 (0.00%)   | 0 / 9 (0.00%)     | 0 / 9 (0.00%)     |
| occurrences (all)                                     | 0                | 0                 | 0                 |
| General disorders and administration site conditions  |                  |                   |                   |
| Administration site bruise                            |                  |                   |                   |
| subjects affected / exposed                           | 0 / 16 (0.00%)   | 0 / 9 (0.00%)     | 0 / 9 (0.00%)     |
| occurrences (all)                                     | 0                | 0                 | 0                 |
| Administration site pain                              |                  |                   |                   |
| subjects affected / exposed                           | 0 / 16 (0.00%)   | 0 / 9 (0.00%)     | 0 / 9 (0.00%)     |
| occurrences (all)                                     | 0                | 0                 | 0                 |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Asthenia  |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Fatigue   |                |                |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 4              | 0              | 0              |
| Gait disturbance                                |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Influenza like illness                          |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Injection site pain                             |                |                |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Pain  |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Puncture site haemorrhage                       |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Vessel puncture site bruise                     |                |                |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Vessel puncture site pain                       |                |                |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Reproductive system and breast disorders        |                |                |                |
| Ovarian cyst                                    |                |                |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Dyspnoea  |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Epistaxis                                       |                |                |                |

|                             |                 |                |                |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Rhinorrhea                  |                 |                |                |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Psychiatric disorders       |                 |                |                |
| Affect lability             |                 |                |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 1 / 9 (11.11%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0              |
| Anxiety                     |                 |                |                |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)           | 3               | 0              | 0              |
| Bradypnea                   |                 |                |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Delirium                    |                 |                |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Depression                  |                 |                |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 1 / 9 (11.11%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0              |
| Depression suicidal         |                 |                |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)           | 0               | 0              | 1              |
| Emotional disorder          |                 |                |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Insomnia                    |                 |                |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)           | 0               | 0              | 1              |
| Irritability                |                 |                |                |
| subjects affected / exposed | 1 / 16 (6.25%)  | 1 / 9 (11.11%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 1               | 1              | 0              |
| Restlessness                |                 |                |                |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |

|  |                |                |                |
|--|----------------|----------------|----------------|
| Investigations                                 |                |                |                |
| Blood bilirubin increased                      |                |                |                |
| subjects affected / exposed                    | 1 / 16 (6.25%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                              | 1              | 0              | 0              |
| Blood creatine phosphokinase increased         |                |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| CSF lymphocyte count increase                  |                |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| CSF protein increased                          |                |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| CSF white blood cell count increased           |                |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Haemoglobin decreased                          |                |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Hepatic enzyme increased                       |                |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 1              | 0              |
| Lymphocyte count decreased                     |                |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Neutrophil count increased                     |                |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Platelet count increased                       |                |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                              | 0              | 0              | 1              |
| White blood cell count increased               |                |                |                |
| subjects affected / exposed                    | 1 / 16 (6.25%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                              | 1              | 0              | 0              |
| Injury, poisoning and procedural complications |                |                |                |

|                               |                 |                |                |
|-------------------------------|-----------------|----------------|----------------|
| Contusion                     |                 |                |                |
| subjects affected / exposed   | 1 / 16 (6.25%)  | 1 / 9 (11.11%) | 0 / 9 (0.00%)  |
| occurrences (all)             | 2               | 1              | 0              |
| Eye contusion                 |                 |                |                |
| subjects affected / exposed   | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)             | 0               | 0              | 0              |
| Fall                          |                 |                |                |
| subjects affected / exposed   | 0 / 16 (0.00%)  | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all)             | 0               | 2              | 2              |
| Foot fracture                 |                 |                |                |
| subjects affected / exposed   | 1 / 16 (6.25%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)             | 1               | 0              | 0              |
| Hand fracture                 |                 |                |                |
| subjects affected / exposed   | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)             | 0               | 0              | 0              |
| Head injury                   |                 |                |                |
| subjects affected / exposed   | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)             | 0               | 0              | 1              |
| Post lumbar puncture syndrome |                 |                |                |
| subjects affected / exposed   | 2 / 16 (12.50%) | 1 / 9 (11.11%) | 2 / 9 (22.22%) |
| occurrences (all)             | 3               | 2              | 2              |
| Post procedural contusion     |                 |                |                |
| subjects affected / exposed   | 1 / 16 (6.25%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)             | 1               | 0              | 0              |
| Post procedural discomfort    |                 |                |                |
| subjects affected / exposed   | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)             | 0               | 0              | 1              |
| Procedural headache           |                 |                |                |
| subjects affected / exposed   | 0 / 16 (0.00%)  | 1 / 9 (11.11%) | 0 / 9 (0.00%)  |
| occurrences (all)             | 0               | 1              | 0              |
| Procedural nausea             |                 |                |                |
| subjects affected / exposed   | 1 / 16 (6.25%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)             | 1               | 0              | 0              |
| Procedural pain               |                 |                |                |
| subjects affected / exposed   | 3 / 16 (18.75%) | 0 / 9 (0.00%)  | 2 / 9 (22.22%) |
| occurrences (all)             | 6               | 0              | 5              |

|   |                      |                     |                     |
|---|----------------------|---------------------|---------------------|
| Procedural vomiting<br>subjects affected / exposed<br>occurrences (all) | 1 / 16 (6.25%)<br>1  | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Thermal burn<br>subjects affected / exposed<br>occurrences (all)        | 0 / 16 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Wound<br>subjects affected / exposed<br>occurrences (all)               | 0 / 16 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Nervous system disorders  |                      |                     |                     |
| Amnesia<br>subjects affected / exposed<br>occurrences (all)             | 0 / 16 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Ataxia<br>subjects affected / exposed<br>occurrences (all)              | 0 / 16 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Balance disorder<br>subjects affected / exposed<br>occurrences (all)    | 0 / 16 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Chorea<br>subjects affected / exposed<br>occurrences (all)              | 1 / 16 (6.25%)<br>1  | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)           | 0 / 16 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 | 0 / 9 (0.00%)<br>0  |
| Dysarthria<br>subjects affected / exposed<br>occurrences (all)          | 0 / 16 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)           | 0 / 16 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Headache<br>subjects affected / exposed<br>occurrences (all)            | 5 / 16 (31.25%)<br>7 | 0 / 9 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 |
| Hyperreflexia   |                      |                     |                     |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed          | 0 / 16 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |
| Hypoaesthesia                        |                |                |                |
| subjects affected / exposed          | 1 / 16 (6.25%) | 1 / 9 (11.11%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 1              | 1              | 0              |
| Hyporeflexia                         |                |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Lethargy                             |                |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Lumbosacral radiculopathy            |                |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |
| Migraine                             |                |                |                |
| subjects affected / exposed          | 1 / 16 (6.25%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0              |
| Paraesthesia                         |                |                |                |
| subjects affected / exposed          | 1 / 16 (6.25%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                    | 2              | 0              | 0              |
| Pleocytosis                          |                |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |
| Post-traumatic headache              |                |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |
| Radicular pain                       |                |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%) | 0 / 9 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Sensory disturbance                  |                |                |                |
| subjects affected / exposed          | 1 / 16 (6.25%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0              |
| Syncope                              |                |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |
| Blood and lymphatic system disorders |                |                |                |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 16 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 16 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 |
| Ear and labyrinth disorders<br>Ear discomfort<br>subjects affected / exposed<br>occurrences (all)      | 0 / 16 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Eye disorders<br>Dry eye<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 16 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Gastrointestinal disorders<br>Constipation<br>subjects affected / exposed<br>occurrences (all)         | 0 / 16 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)  | 1 / 16 (6.25%)<br>1 | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)   | 1 / 16 (6.25%)<br>2 | 1 / 9 (11.11%)<br>1 | 0 / 9 (0.00%)<br>0  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)   | 0 / 16 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 | 0 / 9 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders<br>Alopecia<br>subjects affected / exposed<br>occurrences (all) | 1 / 16 (6.25%)<br>1 | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Dermatitis contact<br>subjects affected / exposed<br>occurrences (all)                                 | 1 / 16 (6.25%)<br>2 | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Rash vesicular<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 16 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| Renal and urinary disorders                     |                 |                |                |
| Haematuria                                      |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                               | 0               | 0              | 1              |
| Urinary retention                               |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Musculoskeletal and connective tissue disorders |                 |                |                |
| Arthralgia                                      |                 |                |                |
| subjects affected / exposed                     | 2 / 16 (12.50%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 2               | 0              | 0              |
| Back pain                                       |                 |                |                |
| subjects affected / exposed                     | 3 / 16 (18.75%) | 3 / 9 (33.33%) | 1 / 9 (11.11%) |
| occurrences (all)                               | 4               | 4              | 1              |
| Limb discomfort                                 |                 |                |                |
| subjects affected / exposed                     | 1 / 16 (6.25%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 1               | 0              | 0              |
| Muscle spasms                                   |                 |                |                |
| subjects affected / exposed                     | 2 / 16 (12.50%) | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 2               | 0              | 0              |
| Muscular weakness                               |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Musculoskeletal pain                            |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 1 / 9 (11.11%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0               | 1              | 0              |
| Musculoskeletal stiffness                       |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Neck pain                                       |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 9 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Osteoarthritis                                  |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all)                               | 0               | 1              | 1              |
| Pain in extremity                               |                 |                |                |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 1 / 16 (6.25%)<br>1 | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Spinal pain<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 16 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| <b>Infections and infestations</b>  |                     |                     |                     |
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 16 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 |
| Ear infection<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 16 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 16 (6.25%)<br>1 | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Lower respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)       | 0 / 16 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)             | 0 / 16 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)       | 1 / 16 (6.25%)<br>1 | 1 / 9 (11.11%)<br>1 | 0 / 9 (0.00%)<br>0  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 16 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 16 (6.25%)<br>3 | 2 / 9 (22.22%)<br>2 | 1 / 9 (11.11%)<br>1 |
| <b>Metabolism and nutrition disorders</b>   |                     |                     |                     |
| Increased appetite<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 16 (6.25%)<br>1 | 0 / 9 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |

|                                   |                   |                    |                    |
|-----------------------------------|-------------------|--------------------|--------------------|
| <b>Non-serious adverse events</b> | WVE-120101 (8 mg) | WVE-120101 (16 mg) | WVE-120101 (32 mg) |
|-----------------------------------|-------------------|--------------------|--------------------|

| Total subjects affected by non-serious adverse events<br>subjects affected / exposed | 9 / 9 (100.00%) | 7 / 8 (87.50%) | 9 / 10 (90.00%) |
|--|-----------------|----------------|-----------------|
| <b>Vascular disorders</b>  |                 |                |                 |
| Flushing   |                 |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%)   | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)  | 0               | 0              | 0               |
| Hot flush  |                 |                |                 |
| subjects affected / exposed  | 1 / 9 (11.11%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)  | 1               | 0              | 0               |
| Hypertension   |                 |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%)   | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)  | 0               | 0              | 0               |
| Hypotension  |                 |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%)   | 1 / 8 (12.50%) | 1 / 10 (10.00%) |
| occurrences (all)  | 0               | 1              | 1               |
| <b>General disorders and administration site conditions</b>                          |                 |                |                 |
| Administration site bruise   |                 |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%)   | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)  | 0               | 1              | 0               |
| Administration site pain   |                 |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%)   | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)  | 0               | 1              | 0               |
| Asthenia   |                 |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%)   | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)  | 0               | 0              | 0               |
| Fatigue  |                 |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%)   | 0 / 8 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)  | 0               | 0              | 2               |
| Gait disturbance   |                 |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%)   | 0 / 8 (0.00%)  | 2 / 10 (20.00%) |
| occurrences (all)  | 0               | 0              | 3               |
| Influenza like illness   |                 |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%)   | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)  | 0               | 1              | 0               |
| Injection site pain  |                 |                |                 |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Puncture site haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 9 (11.11%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Vessel puncture site bruise<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Vessel puncture site pain<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Reproductive system and breast disorders<br>Ovarian cyst<br>subjects affected / exposed<br>occurrences (all)    | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders<br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)   | 1 / 9 (11.11%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)   | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Psychiatric disorders<br>Affect lability<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)   | 1 / 9 (11.11%)<br>1 | 1 / 8 (12.50%)<br>1 | 0 / 10 (0.00%)<br>0 |
| Bradypnea   |                     |                     |                     |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed            | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                      | 0              | 0              | 1               |
| Delirium                               |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                      | 0              | 0              | 1               |
| Depression                             |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Depression suicidal                    |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Emotional disorder                     |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)                      | 0              | 1              | 0               |
| Insomnia                               |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Irritability                           |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)                      | 0              | 1              | 0               |
| Restlessness                           |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Investigations                         |                |                |                 |
| Blood bilirubin increased              |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Blood creatine phosphokinase increased |                |                |                 |
| subjects affected / exposed            | 1 / 9 (11.11%) | 1 / 8 (12.50%) | 1 / 10 (10.00%) |
| occurrences (all)                      | 1              | 1              | 1               |
| CSF lymphocyte count increase          |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                      | 0              | 0              | 1               |
| CSF protein increased                  |                |                |                 |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0              | 1              | 0               |
| CSF white blood cell count increased           |                |                |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0               |
| Haemoglobin decreased                          |                |                |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0               |
| Hepatic enzyme increased                       |                |                |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0               |
| Lymphocyte count decreased                     |                |                |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                              | 0              | 0              | 1               |
| Neutrophil count increased                     |                |                |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                              | 0              | 0              | 1               |
| Platelet count increased                       |                |                |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0               |
| White blood cell count increased               |                |                |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                              | 0              | 0              | 1               |
| Injury, poisoning and procedural complications |                |                |                 |
| Contusion                                      |                |                |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0               |
| Eye contusion                                  |                |                |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                              | 0              | 0              | 1               |
| Fall   |                |                |                 |
| subjects affected / exposed                    | 1 / 9 (11.11%) | 2 / 8 (25.00%) | 1 / 10 (10.00%) |
| occurrences (all)                              | 1              | 2              | 1               |
| Foot fracture                                  |                |                |                 |

|                               |                |                |                 |
|-------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Hand fracture                 |                |                |                 |
| subjects affected / exposed   | 1 / 9 (11.11%) | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)             | 1              | 0              | 0               |
| Head injury                   |                |                |                 |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Post lumbar puncture syndrome |                |                |                 |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)             | 0              | 1              | 0               |
| Post procedural contusion     |                |                |                 |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Post procedural discomfort    |                |                |                 |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Procedural headache           |                |                |                 |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Procedural nausea             |                |                |                 |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Procedural pain               |                |                |                 |
| subjects affected / exposed   | 3 / 9 (33.33%) | 1 / 8 (12.50%) | 2 / 10 (20.00%) |
| occurrences (all)             | 5              | 1              | 2               |
| Procedural vomiting           |                |                |                 |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Thermal burn                  |                |                |                 |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)             | 0              | 1              | 0               |
| Wound                         |                |                |                 |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)             | 0              | 1              | 0               |
| Nervous system disorders      |                |                |                 |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| Amnesia                     |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0              | 1               |
| Ataxia                      |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0              | 1               |
| Balance disorder            |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 8 (12.50%) | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 1              | 1               |
| Chorea                      |                |                |                 |
| subjects affected / exposed | 2 / 9 (22.22%) | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 2              | 0              | 0               |
| Dizziness                   |                |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 8 (12.50%) | 4 / 10 (40.00%) |
| occurrences (all)           | 3              | 1              | 5               |
| Dysarthria                  |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 2 / 10 (20.00%) |
| occurrences (all)           | 0              | 0              | 2               |
| Dysgeusia                   |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Headache                    |                |                |                 |
| subjects affected / exposed | 2 / 9 (22.22%) | 2 / 8 (25.00%) | 4 / 10 (40.00%) |
| occurrences (all)           | 4              | 7              | 4               |
| Hyperreflexia               |                |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Hypoaesthesia               |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Hyporeflexia                |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0              | 1               |
| Lethargy                    |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| Lumbosacral radiculopathy<br>subjects affected / exposed<br>occurrences (all) | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Migraine<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Paraesthesia<br>subjects affected / exposed<br>occurrences (all)              | 1 / 9 (11.11%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Pleocytosis<br>subjects affected / exposed<br>occurrences (all)               | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Post-traumatic headache<br>subjects affected / exposed<br>occurrences (all)   | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Radicular pain<br>subjects affected / exposed<br>occurrences (all)            | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Sensory disturbance<br>subjects affected / exposed<br>occurrences (all)       | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Syncope<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Blood and lymphatic system disorders  |                     |                     |                     |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)                | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)          | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Ear and labyrinth disorders   |                     |                     |                     |
| Ear discomfort<br>subjects affected / exposed<br>occurrences (all)            | 0 / 9 (0.00%)<br>0  | 1 / 8 (12.50%)<br>2 | 0 / 10 (0.00%)<br>0 |
| Eye disorders   |                     |                     |                     |

|  |                     |                     |                      |
|--|---------------------|---------------------|----------------------|
| Dry eye<br>subjects affected / exposed<br>occurrences (all)            | 1 / 9 (11.11%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Gastrointestinal disorders   |                     |                     |                      |
| Constipation<br>subjects affected / exposed<br>occurrences (all)       | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)          | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)             | 1 / 9 (11.11%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)           | 1 / 9 (11.11%)<br>1 | 1 / 8 (12.50%)<br>1 | 0 / 10 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders                                 |                     |                     |                      |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)           | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Dermatitis contact<br>subjects affected / exposed<br>occurrences (all) | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Rash vesicular<br>subjects affected / exposed<br>occurrences (all)     | 1 / 9 (11.11%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Renal and urinary disorders  |                     |                     |                      |
| Haematuria<br>subjects affected / exposed<br>occurrences (all)         | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Urinary retention<br>subjects affected / exposed<br>occurrences (all)  | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Musculoskeletal and connective tissue disorders                        |                     |                     |                      |
| Arthralgia   |                     |                     |                      |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0              | 1               |
| Back pain                   |                |                |                 |
| subjects affected / exposed | 2 / 9 (22.22%) | 3 / 8 (37.50%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 4              | 4              | 0               |
| Limb discomfort             |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Muscle spasms               |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Muscular weakness           |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0              | 1               |
| Musculoskeletal pain        |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Musculoskeletal stiffness   |                |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Neck pain                   |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Osteoarthritis              |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Pain in extremity           |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Spinal pain                 |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Infections and infestations |                |                |                 |
| Conjunctivitis              |                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| Ear infection                           |                |                |                 |
| subjects affected / exposed             | 0 / 9 (0.00%)  | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)                       | 0              | 1              | 0               |
| Influenza                               |                |                |                 |
| subjects affected / exposed             | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                       | 0              | 0              | 0               |
| Lower respiratory tract infection       |                |                |                 |
| subjects affected / exposed             | 1 / 9 (11.11%) | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                       | 1              | 0              | 0               |
| Respiratory tract infection             |                |                |                 |
| subjects affected / exposed             | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                       | 0              | 0              | 0               |
| Upper respiratory tract infection       |                |                |                 |
| subjects affected / exposed             | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                       | 0              | 0              | 0               |
| Urinary tract infection                 |                |                |                 |
| subjects affected / exposed             | 1 / 9 (11.11%) | 0 / 8 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                       | 1              | 0              | 1               |
| Viral upper respiratory tract infection |                |                |                 |
| subjects affected / exposed             | 1 / 9 (11.11%) | 1 / 8 (12.50%) | 0 / 10 (0.00%)  |
| occurrences (all)                       | 1              | 1              | 0               |
| Metabolism and nutrition disorders      |                |                |                 |
| Increased appetite                      |                |                |                 |
| subjects affected / exposed             | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                       | 0              | 0              | 0               |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 29 August 2018  | <ul style="list-style-type: none"><li>• Implemented edits made in United Kingdom versions 0.1 and 0.2, and made minor clarifications and corrections.</li><li>• Allowed patients to enter directly into the multiple-dose portion of the study. A separate schedule of assessments was added for these patients.</li><li>• Added objective criteria for individual stopping criteria in the multiple-dose phase per Regulatory feedback.</li><li>• Extended the washout required for other investigational agents to a minimum of 1 year.</li></ul>   |
| 21 January 2020 | <ul style="list-style-type: none"><li>• Added the 32 mg cohort to the study.</li><li>• For the 32 mg cohort, the washout period after a single dose was 4 weeks (instead of 8 weeks) based on available nonclinical and clinical data to date. A new schedule of assessments specific to the 32 mg cohort was added to account for this.</li><li>• Change in the inclusion criterion for body mass index (ie, <math>\leq 30</math> changed to <math>\leq 32</math>).</li><li>• Addition of new urine sample PK assessments.</li><li>• New electrocardiogram data collection timepoints.</li></ul> |

Notes:

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### 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 treatment or dose escalation.

Notes: