



## Clinical trial results:

### A Multicenter, Randomized, Double-blind, Placebo-controlled, Phase 1b/2a Study of WVE-120102 Administered Intrathecally in Patients with Huntington's Disease

#### Summary

EudraCT number	2016-005142-39
Trial protocol	GB DK FR DE
Global end of trial date	10 May 2021

#### Results information

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

#### Trial information

##### Trial identification

Sponsor protocol code	WVE-HDSNP2-001
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03225846
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	10 May 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 May 2021
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 October 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: 9
Country: Number of subjects enrolled	Canada: 26
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Poland: 13
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 25
Worldwide total number of subjects	88
EEA total number of subjects	24

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)	86
From 65 to 84 years	2
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 rs362331. Following completion of this study, eligible patients were enrolled in an open-label extension study (WVE-HDSNP2-002).

### 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 88 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-120102 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-120102 (2 milligram [mg])
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Arm description:

WVE-120102: WVE-120102 is a stereopure antisense oligonucleotide (ASO).

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

Dosage and administration details:

WVE-120102 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-120102 (4 mg)
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Arm description:

WVE-120102: WVE-120102 is a stereopure ASO.

Arm type	Experimental
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Investigational medicinal product name	WVE-120102
Investigational medicinal product code	WVE-120102
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use
Dosage and administration details:	
WVE-120102 4 mg 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-120102 (8 mg)
Arm description:	
WVE-120102: WVE-120102 is a stereopure ASO.	
Arm type	Experimental
Investigational medicinal product name	WVE-120102
Investigational medicinal product code	WVE-120102
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use
Dosage and administration details:	
WVE-120102 8 mg 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-120102 (12 mg)
Arm description:	
WVE-120102: WVE-120102 is a stereopure ASO.	
Arm type	Experimental
Investigational medicinal product name	WVE-120102
Investigational medicinal product code	WVE-120102
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use
Dosage and administration details:	
WVE-120102 12 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-120102 (16 mg)
Arm description:	
WVE-120102: WVE-120102 is a stereopure ASO.	
Arm type	Experimental
Investigational medicinal product name	WVE-120102
Investigational medicinal product code	WVE-120102
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use
Dosage and administration details:	
WVE-120102 16 mg 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-120102 (32 mg)
Arm description:	
WVE-120102: WVE-120102 is a stereopure ASO.	
Arm type	Experimental

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

Dosage and administration details:

WVE-120102 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.

Number of subjects in period 1	Pooled Placebo	WVE-120102 (2 milligram [mg])	WVE-120102 (4 mg)
Started	22	9	12
Single Dose Period Only	6 <sup>[1]</sup>	3 <sup>[2]</sup>	4 <sup>[3]</sup>
Multiple Dose Period Only	3 <sup>[4]</sup>	0 <sup>[5]</sup>	3 <sup>[6]</sup>
Single Dose and Multiple Dose Periods	13 <sup>[7]</sup>	6 <sup>[8]</sup>	5 <sup>[9]</sup>
Completed	22	7	11
Not completed	0	2	1
Consent withdrawn by subject	-	1	-
Patient decision	-	-	-
Adverse event, non-fatal	-	-	-
Death	-	1	-
Patient did not wish to comply with eligibility	-	-	1

Number of subjects in period 1	WVE-120102 (8 mg)	WVE-120102 (12 mg)	WVE-120102 (16 mg)
Started	15	8	9
Single Dose Period Only	7 <sup>[10]</sup>	8	0 <sup>[11]</sup>
Multiple Dose Period Only	6 <sup>[12]</sup>	0 <sup>[13]</sup>	0 <sup>[14]</sup>
Single Dose and Multiple Dose Periods	2 <sup>[15]</sup>	0 <sup>[16]</sup>	9
Completed	15	8	9
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Patient decision	-	-	-
Adverse event, non-fatal	-	-	-
Death	-	-	-
Patient did not wish to comply with eligibility	-	-	-

Number of subjects in period 1	WVE-120102 (32 mg)
Started	13
Single Dose Period Only	4 <sup>[17]</sup>
Multiple Dose Period Only	4 <sup>[18]</sup>
Single Dose and Multiple Dose Periods	5 <sup>[19]</sup>

Completed	6
Not completed	7
Consent withdrawn by subject	-
Patient decision	1
Adverse event, non-fatal	6
Death	-
Patient did not wish to comply with eligibility	-

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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.

[11] - 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.

[12] - 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.

[13] - 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.

[14] - 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.

[15] - 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.

[16] - 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.

[17] - 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.

[18] - 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.

[19] - 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

### Reporting groups

Reporting group title	Pooled Placebo
Reporting group description: Placebo: 0.9% Sodium Chloride.	
Reporting group title	WVE-120102 (2 milligram [mg])
Reporting group description: WVE-120102: WVE-120102 is a stereopure antisense oligonucleotide (ASO).	
Reporting group title	WVE-120102 (4 mg)
Reporting group description: WVE-120102: WVE-120102 is a stereopure ASO.	
Reporting group title	WVE-120102 (8 mg)
Reporting group description: WVE-120102: WVE-120102 is a stereopure ASO.	
Reporting group title	WVE-120102 (12 mg)
Reporting group description: WVE-120102: WVE-120102 is a stereopure ASO.	
Reporting group title	WVE-120102 (16 mg)
Reporting group description: WVE-120102: WVE-120102 is a stereopure ASO.	
Reporting group title	WVE-120102 (32 mg)
Reporting group description: WVE-120102: WVE-120102 is a stereopure ASO.	

Reporting group values	Pooled Placebo	WVE-120102 (2 milligram [mg])	WVE-120102 (4 mg)
Number of subjects	22	9	12
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	46.8 ± 10.16	52.4 ± 11.59	46 ± 10.63
Gender categorical Units: Subjects			
Female	8	5	7
Male	14	4	5
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	21	9	12
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	22	9	12
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment			
Units: Subjects			
Australia	2	0	0
Canada	9	8	2
Denmark	0	0	2
France	0	0	0
Germany	1	0	0
Poland	4	0	4
United Kingdom	0	0	1
United States	6	1	3
Diagnosis stage			
Units: Subjects			
Stage 1	9	5	6
Stage 2	13	4	6
Time since initial diagnosis			
Units: years			
arithmetic mean	6.1	9.9	3.8
standard deviation	± 5.95	± 8.80	± 3.62
Age at disease onset			
Units: years			
arithmetic mean	40.18	42.00	41.75
standard deviation	± 10.527	± 16.363	± 12.129

<b>Reporting group values</b>	WVE-120102 (8 mg)	WVE-120102 (12 mg)	WVE-120102 (16 mg)
Number of subjects	15	8	9
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	49.3	47.1	53.1
standard deviation	± 10.40	± 8.48	± 8.33
Gender categorical			
Units: Subjects			
Female	10	4	2
Male	5	4	7
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	15	8	9
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	15	8	9
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment			
Units: Subjects			
Australia	0	0	0
Canada	1	0	6
Denmark	3	0	0
France	0	0	0
Germany	0	0	0
Poland	3	0	1
United Kingdom	1	0	2
United States	7	8	0
Diagnosis stage			
Units: Subjects			
Stage 1	8	1	5
Stage 2	7	7	4
Time since initial diagnosis			
Units: years			
arithmetic mean	5.6	3.9	3.2
standard deviation	± 2.80	± 3.23	± 5.61
Age at disease onset			
Units: years			
arithmetic mean	43.33	42.50	49.00
standard deviation	± 9.378	± 9.289	± 6.652

<b>Reporting group values</b>	WVE-120102 (32 mg)	Total	
Number of subjects	13	88	
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	54.1		
standard deviation	± 8.88	-	
Gender categorical			
Units: Subjects			
Female	6	42	
Male	7	46	
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	1	
Not Hispanic or Latino	13	87	
Unknown or Not Reported	0	0	
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	

Black or African American	0	0	
White	13	88	
More than one race	0	0	
Unknown or Not Reported	0	0	
Region of Enrollment			
Units: Subjects			
Australia	7	9	
Canada	0	26	
Denmark	0	5	
France	1	1	
Germany	4	5	
Poland	1	13	
United Kingdom	0	4	
United States	0	25	
Diagnosis stage			
Units: Subjects			
Stage 1	11	45	
Stage 2	2	43	
Time since initial diagnosis			
Units: years			
arithmetic mean	5.6		
standard deviation	± 9.28	-	
Age at disease onset			
Units: years			
arithmetic mean	48.08		
standard deviation	± 12.796	-	

## End points

### End points reporting groups

Reporting group title	Pooled Placebo
Reporting group description: Placebo: 0.9% Sodium Chloride.	
Reporting group title	WVE-120102 (2 milligram [mg])
Reporting group description: WVE-120102: WVE-120102 is a stereopure antisense oligonucleotide (ASO).	
Reporting group title	WVE-120102 (4 mg)
Reporting group description: WVE-120102: WVE-120102 is a stereopure ASO.	
Reporting group title	WVE-120102 (8 mg)
Reporting group description: WVE-120102: WVE-120102 is a stereopure ASO.	
Reporting group title	WVE-120102 (12 mg)
Reporting group description: WVE-120102: WVE-120102 is a stereopure ASO.	
Reporting group title	WVE-120102 (16 mg)
Reporting group description: WVE-120102: WVE-120102 is a stereopure ASO.	
Reporting group title	WVE-120102 (32 mg)
Reporting group description: WVE-120102: WVE-120102 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: 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-120102 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: 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-120102 (2 milligram [mg])	WVE-120102 (4 mg)	WVE-120102 (8 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	9	12	15
Units: patients	20	8	9	13

End point values	WVE-120102 (12 mg)	WVE-120102 (16 mg)	WVE-120102 (32 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	9	13	
Units: patients	4	8	13	

## 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>
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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-120102 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
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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-120102 (2 milligram [mg])	WVE-120102 (4 mg)	WVE-120102 (8 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	9	12	15
Units: patients	2	1	1	2

End point values	WVE-120102 (12 mg)	WVE-120102 (16 mg)	WVE-120102 (32 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	9	13	
Units: patients	0	2	9	

## 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-120102 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-120102 (2 milligram [mg])	WVE-120102 (4 mg)	WVE-120102 (8 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	9	12	15
Units: patients	0	1	2	2

End point values	WVE-120102 (12 mg)	WVE-120102 (16 mg)	WVE-120102 (32 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	9	13	
Units: patients	0	0	9	

## 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-120102 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-120102 (2 milligram [mg])	WVE-120102 (4 mg)	WVE-120102 (8 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	9	12	15
Units: patients	0	0	0	0

End point values	WVE-120102 (12 mg)	WVE-120102 (16 mg)	WVE-120102 (32 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	9	13	
Units: patients	0	0	6	

## 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>
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End point description:

Cmax of WVE-120102 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-120102 concentration measurement. Here, n= number of patients analyzed at specific timepoint and '99999'= not applicable as no patient was analyzed.

End point type	Secondary
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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-120102 were evaluated for this PK end point. All patients enrolled in reporting group "WVE-120102 (12 mg)" were treated only in single dose period. Therefore, no patients were evaluated for this PK end point.

End point values	WVE-120102 (2 milligram [mg])	WVE-120102 (4 mg)	WVE-120102 (8 mg)	WVE-120102 (16 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	12	15	9
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 1 (n= 9, 9, 9, 9, 8)	1.35 (± 2.714)	8.54 (± 6.073)	29.87 (± 31.891)	31.49 (± 15.801)
Day 112 (n= 6, 8, 8, 9, 0)	7.46 (± 15.411)	15.55 (± 14.587)	36.16 (± 30.012)	59.49 (± 35.718)

End point values	WVE-120102 (32 mg)			
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Subject group type	Reporting group			
Number of subjects analysed	11			
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 1 (n= 9, 9, 9, 9, 8)	96.21 (± 57.394)			
Day 112 (n= 6, 8, 8, 9, 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-120102 in plasma. The PK population included all treated patients in the safety population with at least 1 post-dose plasma or CSF WVE-120102 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-120102 were evaluated for this PK end point. All patients enrolled in reporting group "WVE-120102 (12 mg)" were treated only in single dose period. Therefore, no patients were evaluated for this PK end point.

End point values	WVE-120102 (2 milligram [mg])	WVE-120102 (4 mg)	WVE-120102 (8 mg)	WVE-120102 (16 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	12	15	9
Units: hour				
arithmetic mean (standard deviation)				
Day 1 (n= 9, 9, 9, 9, 8)	3.33 (± 7.742)	1.26 (± 1.044)	1.77 (± 1.101)	1.77 (± 1.345)
Day 112 (n= 6, 8, 8, 9, 0)	1.22 (± 0.314)	1.86 (± 0.874)	2.06 (± 1.206)	1.98 (± 0.828)

End point values	WVE-120102 (32 mg)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: hour				
arithmetic mean (standard deviation)				
Day 1 (n= 9, 9, 9, 9, 8)	3.09 (± 3.752)			
Day 112 (n= 6, 8, 8, 9, 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
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End point description:

AUClast from time 0 to the last quantifiable concentration of WVE-120102 in plasma. The PK population included all treated patients in the safety population with at least 1 post-dose plasma or CSF WVE-120102 concentration measurement. Here, n= number of patients analyzed at specific timepoint and '99999'= not applicable as no patient was analyzed.

End point type	Secondary
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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-120102 were evaluated for this PK end point. All patients enrolled in reporting group "WVE-120102 (12 mg)" were treated only in single dose period. Therefore, no patients were evaluated for this PK end point.

End point values	WVE-120102 (2 milligram [mg])	WVE-120102 (4 mg)	WVE-120102 (8 mg)	WVE-120102 (16 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	12	15	9
Units: hour*ng/mL				
arithmetic mean (standard deviation)				
Day 1 (n= 2, 7, 8, 8, 8)	24.65 (± 9.108)	62.05 (± 67.358)	132.44 (± 91.913)	804.92 (± 1456.786)
Day 112 (n= 2, 7, 7, 9, 0)	23.83 (± 23.187)	35.47 (± 22.280)	107.83 (± 70.198)	133.22 (± 67.683)

End point values	WVE-120102 (32 mg)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: hour*ng/mL				
arithmetic mean (standard deviation)				
Day 1 (n= 2, 7, 8, 8, 8)	919.14 (± 271.997)			
Day 112 (n= 2, 7, 7, 9, 0)	99999 (± 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>
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End point description:

Elimination rate of WVE-120102 from plasma ( $t_{1/2}$ ). The PK population included all treated patients in the safety population with at least 1 post-dose plasma or CSF WVE-120102 concentration measurement. Here, 9999 = standard deviation is not applicable with an  $n=1$ .

End point type	Secondary
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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: All patients enrolled in reporting group "WVE-120102 (12 mg)" were treated only in single dose period. Therefore, no patients were evaluated for this end point.

End point values	WVE-120102 (2 milligram [mg])	WVE-120102 (4 mg)	WVE-120102 (8 mg)	WVE-120102 (16 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 <sup>[9]</sup>	2	1	5
Units: hour				
arithmetic mean (standard deviation)	()	33.42 ( $\pm$ 30.983)	6.23 ( $\pm$ 9999)	13.45 ( $\pm$ 4.604)

Notes:

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

End point values	WVE-120102 (32 mg)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hour				
arithmetic mean (standard deviation)	18.17 ( $\pm$ 20.969)			

## Statistical analyses

No statistical analyses for this end point

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

End point title	Pharmacodynamics (PD): Percent Change From Baseline in the Concentration of Mutant Huntingtin (mHTT) Protein at the Last Measured Observation <sup>[10]</sup>
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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-120102 or placebo.

End point type	Secondary
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End point timeframe:

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

Notes:

[10] - 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: All patients enrolled in reporting group "WVE-120102 (12 mg)" were treated only in single dose period. Therefore, no patients were evaluated for this PD end point.

End point values	Pooled Placebo	WVE-120102 (2 milligram [mg])	WVE-120102 (4 mg)	WVE-120102 (8 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	6	8	8
Units: percent change				
median (inter-quartile range (Q1-Q3))	-2.64 (-14.89 to 11.71)	3.46 (-7.67 to 7.80)	-3.53 (-4.20 to 2.41)	-3.45 (-6.46 to 7.35)

End point values	WVE-120102 (16 mg)	WVE-120102 (32 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: percent change				
median (inter-quartile range (Q1-Q3))	-5.82 (-12.09 to 6.44)	-2.06 (-28.72 to 7.84)		

## 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 <sup>[11]</sup>
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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-120102 or placebo.

End point type	Secondary
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End point timeframe:

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

Notes:

[11] - 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: All patients enrolled in reporting group "WVE-120102 (12 mg)" were treated only in single dose period. Therefore, no patients were evaluated for this end point.

<b>End point values</b>	Pooled Placebo	WVE-120102 (2 milligram [mg])	WVE-120102 (4 mg)	WVE-120102 (8 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	6	8	8
Units: percent change				
median (inter-quartile range (Q1-Q3))	0.0 (0.00 to 0.00)	0.0 (-2.00 to 0.00)	0.0 (0.00 to 0.00)	-4.17 (-13.89 to 0.00)

<b>End point values</b>	WVE-120102 (16 mg)	WVE-120102 (32 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: percent change				
median (inter-quartile range (Q1-Q3))	-8.33 (-16.67 to 0.00)	0.0 (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-120102 or placebo.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	8.2
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### Reporting groups

Reporting group title	Pooled Placebo
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Reporting group description:

Placebo: 0.9% Sodium Chloride.

Reporting group title	WVE-120102 (2 mg)
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Reporting group description:

WVE-120102: WVE-120102 is a stereopure ASO.

Reporting group title	WVE-120102 (4 mg)
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Reporting group description:

WVE-120102: WVE-120102 is a stereopure ASO.

Reporting group title	WVE-120102 (8 mg)
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Reporting group description:

WVE-120102: WVE-120102 is a stereopure ASO.

Reporting group title	WVE-120102 (12 mg)
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Reporting group description:

WVE-120102: WVE-120102 is a stereopure ASO.

Reporting group title	WVE-120102 (16 mg)
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Reporting group description:

WVE-120102: WVE-120102 is a stereopure ASO.

Reporting group title	WVE-120102 (32 mg)
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Reporting group description:

WVE-120102: WVE-120102 is a stereopure ASO.

Serious adverse events	Pooled Placebo	WVE-120102 (2 mg)	WVE-120102 (4 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	2 / 12 (16.67%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Injury, poisoning and procedural complications			
Accident at work			

subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (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
Subdural hematoma			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 12 (8.33%)
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			
Amnesia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (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
Ataxia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (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
Cerebellar ataxia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (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 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (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
Syncope			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertigo CNS origin			

subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (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 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (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
Completed suicide			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Confusional State			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (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
Conversion disorder			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (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
Delirium			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (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
Disorientation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (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



Psychotic Disorder			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Meningitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (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-120102 (8 mg)	WVE-120102 (12 mg)	WVE-120102 (16 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)	0 / 8 (0.00%)	0 / 9 (0.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Injury, poisoning and procedural complications			
Accident at work			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Subdural hematoma			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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
Ataxia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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
Cerebellar ataxia			

subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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
Cerebrovascular accident			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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
Syncope			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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
Vertigo CNS origin			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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			
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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 / 15 (0.00%)	0 / 8 (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
Completed suicide			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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

Confusional State			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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
Conversion disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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
Delirium			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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
Disorientation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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
Psychotic Disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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
Infections and infestations			
Meningitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (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-120102 (32 mg)		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 13 (69.23%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Accident at work			

subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subdural hematoma			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Amnesia			
subjects affected / exposed	4 / 13 (30.77%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Ataxia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebellar ataxia			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysarthria			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vertigo CNS origin			

subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Aggression			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Completed suicide			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Confusional State			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Conversion disorder			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Delirium			
subjects affected / exposed	4 / 13 (30.77%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Disorientation			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

Psychotic Disorder			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Meningitis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Pooled Placebo	WVE-120102 (2 mg)	WVE-120102 (4 mg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 22 (90.91%)	8 / 9 (88.89%)	9 / 12 (75.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Varicose vein			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 22 (13.64%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	3	5	0
Gait disturbance			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Influenza like illness			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pain			

subjects affected / exposed	1 / 22 (4.55%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Pyrexia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Choking			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Chronic throat clearing			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Obstructive airways disorder			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Sinus congestion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Psychiatric disorders			

Abnormal behavior			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Anger			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	1 / 22 (4.55%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Apathy			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Depressed mood			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Disorientation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Generalized anxiety disorder			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Irritability			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Mood swings			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Panic attack			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Sleep disorder			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0



Investigations			
Blood creatinine phosphokinase increased			
subjects affected / exposed	2 / 22 (9.09%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Blood fibrinogen increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
C-reactive protein increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
CSF protein increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Chest X-ray abnormal			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Complement factor C3 decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Complement factor C3 increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
White blood cells urine			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Bone contusion			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Chemical burn			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	2 / 22 (9.09%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
Fall			

subjects affected / exposed	3 / 22 (13.64%)	5 / 9 (55.56%)	0 / 12 (0.00%)
occurrences (all)	3	10	0
Joint dislocation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Post lumbar puncture syndrome			
subjects affected / exposed	2 / 22 (9.09%)	0 / 9 (0.00%)	3 / 12 (25.00%)
occurrences (all)	2	0	4
Post procedural complication			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
Post procedural discomfort			
subjects affected / exposed	3 / 22 (13.64%)	1 / 9 (11.11%)	1 / 12 (8.33%)
occurrences (all)	3	2	1
Procedural Pain			
subjects affected / exposed	3 / 22 (13.64%)	2 / 9 (22.22%)	3 / 12 (25.00%)
occurrences (all)	4	4	3
Procedural headache			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rib fracture			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Skin abrasion			
subjects affected / exposed	0 / 22 (0.00%)	5 / 9 (55.56%)	0 / 12 (0.00%)
occurrences (all)	0	6	0
Soft tissue injury			
subjects affected / exposed	0 / 22 (0.00%)	2 / 9 (22.22%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Thermal burn			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Ataxia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cerebellar ataxia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cerebral microhaemorrhage			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Chorea			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Disturbance in attention			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	2 / 22 (9.09%)	2 / 9 (22.22%)	1 / 12 (8.33%)
occurrences (all)	5	5	1
Dizziness postural			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dysarthria			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	8 / 22 (36.36%)	3 / 9 (33.33%)	3 / 12 (25.00%)
occurrences (all)	14	9	3
Hyperaesthesia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 22 (0.00%)	2 / 9 (22.22%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Hyporeflexia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0

Loss of proprioception subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0	1 / 12 (8.33%) 2
Memory impairment subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0	0 / 12 (0.00%) 0
Migraine subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0	1 / 12 (8.33%) 1
Paraesthesia subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	2 / 9 (22.22%) 7	0 / 12 (0.00%) 0
Presyncope subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 3	1 / 9 (11.11%) 1	0 / 12 (0.00%) 0
Reflexes abnormal subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0	0 / 12 (0.00%) 0
Speech disorder subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0	0 / 12 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 9 (0.00%) 0	0 / 12 (0.00%) 0
Tension headache subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0	0 / 12 (0.00%) 0
Ear and labyrinth disorders			
Hyperacusis subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 9 (11.11%) 1	0 / 12 (0.00%) 0
Tinnitus subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0	1 / 12 (8.33%) 1
Vertigo			

subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0	0 / 12 (0.00%) 0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	1 / 22 (4.55%)	1 / 9 (11.11%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
Dry mouth			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Irritable bowel syndrome			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	3 / 22 (13.64%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	3	2	0
Paraesthesia oral			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	8	0
Vomiting			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Blister			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Pruritus generalised			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Nephrolithiasis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Urinary incontinence			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Athralgia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Back pain			
subjects affected / exposed	2 / 22 (9.09%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	4	1	0
Muscle spasms			
subjects affected / exposed	1 / 22 (4.55%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Muscular weakness			

subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
Neck pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Eye infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis viral			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Influenza			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Oral fungal infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	1 / 22 (4.55%)	3 / 9 (33.33%)	0 / 12 (0.00%)
occurrences (all)	1	3	0
Sinusitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	1 / 9 (11.11%) 1	0 / 12 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0	1 / 12 (8.33%) 1
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	2 / 9 (22.22%) 2	4 / 12 (33.33%) 6
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0	0 / 12 (0.00%) 0
Hypercholesterolaemia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0	0 / 12 (0.00%) 0

<b>Non-serious adverse events</b>	WVE-120102 (8 mg)	WVE-120102 (12 mg)	WVE-120102 (16 mg)
Total subjects affected by non-serious adverse events subjects affected / exposed	13 / 15 (86.67%)	4 / 8 (50.00%)	8 / 9 (88.89%)
Vascular disorders			
Hypotension subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	2 / 9 (22.22%) 2
Orthostatic hypotension subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Varicose vein subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Gait disturbance			



subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Choking			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Chronic throat clearing			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Obstructive airways disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Pleural effusion			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Sinus congestion subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Psychiatric disorders			
Abnormal behavior subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Anger subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Anxiety subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	2 / 9 (22.22%) 2
Apathy subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Depressed mood subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Disorientation subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Generalized anxiety disorder subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Irritability subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Mood swings subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1

Panic attack subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Sleep disorder subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Investigations			
Blood creatinine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Blood fibrinogen increased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
C-reactive protein increased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
CSF protein increased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Chest X-ray abnormal subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Complement factor C3 decreased subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Complement factor C3 increased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
White blood cells urine subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Injury, poisoning and procedural complications			
Bone contusion subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Chemical burn			

subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Fall			
subjects affected / exposed	2 / 15 (13.33%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Joint dislocation			
subjects affected / exposed	0 / 15 (0.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Post lumbar puncture syndrome			
subjects affected / exposed	2 / 15 (13.33%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Post procedural complication			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Post procedural discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Procedural Pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	3 / 9 (33.33%)
occurrences (all)	1	0	3
Procedural headache			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Soft tissue injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Thermal burn			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Nervous system disorders			
Amnesia			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Ataxia			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Cerebellar ataxia			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Cerebral microhaemorrhage			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Chorea			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Disturbance in attention			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Dizziness			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	3 / 9 (33.33%) 3
Dizziness postural			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Dysarthria			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Headache			
subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 9	0 / 8 (0.00%) 0	6 / 9 (66.67%) 22
Hyperaesthesia			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1

Hypoaesthesia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Hyporeflexia			
subjects affected / exposed	1 / 15 (6.67%)	2 / 8 (25.00%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
Loss of proprioception			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Memory impairment			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Presyncope			
subjects affected / exposed	0 / 15 (0.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Reflexes abnormal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Speech disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Tension headache			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Hyperacusis			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Tinnitus subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Vertigo subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Eye disorders Dry eye subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Visual acuity reduced subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Gastrointestinal disorders Abdominal hernia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Dry mouth subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Irritable bowel syndrome subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	2 / 9 (22.22%) 3
Paraesthesia oral			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 8 (12.50%) 1	0 / 9 (0.00%) 0
Skin and subcutaneous tissue disorders			
Blister subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Eczema subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Pruritus generalised subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Skin lesion subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Renal and urinary disorders			
Haematuria subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Nephrolithiasis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Urinary incontinence subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Musculoskeletal and connective tissue disorders			
Athralgia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Back pain			



subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	5 / 9 (55.56%)
occurrences (all)	1	0	12
Muscle spasms			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	6
Musculoskeletal stiffness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Plantar fasciitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Eye infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Oral fungal infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Respiratory tract infection subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Sinusitis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
Hypercholesterolaemia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0

<b>Non-serious adverse events</b>	WVE-120102 (32 mg)		
Total subjects affected by non-serious adverse events subjects affected / exposed	13 / 13 (100.00%)		
Vascular disorders Hypotension subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Orthostatic hypotension subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Varicose vein subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
General disorders and administration			

site conditions			
Fatigue			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Gait disturbance			
subjects affected / exposed	3 / 13 (23.08%)		
occurrences (all)	5		
Influenza like illness			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Choking			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Chronic throat clearing			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Obstructive airways disorder			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Oropharyngeal pain			

subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Pleural effusion			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Sinus congestion			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Abnormal behavior			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Anger			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	4		
Apathy			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Depressed mood			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Disorientation			
subjects affected / exposed	3 / 13 (23.08%)		
occurrences (all)	4		
Generalized anxiety disorder			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Irritability			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		

Mood swings subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Panic attack subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Sleep disorder subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Investigations			
Blood creatinine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Blood fibrinogen increased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
C-reactive protein increased subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
CSF protein increased subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Chest X-ray abnormal subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Complement factor C3 decreased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Complement factor C3 increased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
White blood cells urine subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Injury, poisoning and procedural complications			

Bone contusion			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Chemical burn			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Joint dislocation			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Post lumbar puncture syndrome			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Post procedural complication			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Post procedural discomfort			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Procedural Pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Procedural headache			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Rib fracture			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Skin abrasion			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		

Soft tissue injury			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Thermal burn			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Amnesia			
subjects affected / exposed	4 / 13 (30.77%)		
occurrences (all)	4		
Ataxia			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Cerebellar ataxia			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Cerebral microhaemorrhage			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Chorea			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Disturbance in attention			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	5		
Dizziness postural			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Dysarthria			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Headache			

subjects affected / exposed	5 / 13 (38.46%)		
occurrences (all)	6		
Hyperaesthesia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Hyporeflexia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Loss of proprioception			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Memory impairment			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Migraine			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Presyncope			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Reflexes abnormal			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Speech disorder			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Tension headache			



subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Ear and labyrinth disorders			
Hyperacusis			
subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Tinnitus			
subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Vertigo			
subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 3		
Eye disorders			
Dry eye			
subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Visual acuity reduced			
subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Constipation			
subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Diarrhoea			
subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Dry mouth			
subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Irritable bowel syndrome			
subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Nausea			

subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Paraesthesia oral			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Pruritus generalised			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Skin lesion			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Nephrolithiasis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Urinary incontinence			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			

Athralgia subjects affected / exposed occurrences (all)  Back pain subjects affected / exposed occurrences (all)  Muscle spasms subjects affected / exposed occurrences (all)  Muscular weakness subjects affected / exposed occurrences (all)  Musculoskeletal stiffness subjects affected / exposed occurrences (all)  Neck pain subjects affected / exposed occurrences (all)  Pain in extremity subjects affected / exposed occurrences (all)  Plantar fasciitis subjects affected / exposed occurrences (all)	0 / 13 (0.00%)		
	0		
	2 / 13 (15.38%)		
	2		
	0 / 13 (0.00%)		
	0		
	0 / 13 (0.00%)		
	0		
Infections and infestations Eye infection subjects affected / exposed occurrences (all)  Gastroenteritis viral subjects affected / exposed occurrences (all)  Influenza subjects affected / exposed occurrences (all)  Oral fungal infection	0 / 13 (0.00%)		
	0		
	0 / 13 (0.00%)		
	0		
	0 / 13 (0.00%)		
	0		

subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Hypercholesterolaemia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 June 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 in alignment with United States version 0.3.</li><li>• Utilized global language wherever possible in the objectives/endpoints to account for the fact that some regions were doing a single ascending dose (SAD)/multiple ascending dose study while other were doing only an SAD study.</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>• Objective criteria for individual stopping criteria added 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>
17 September 2019	<ul style="list-style-type: none"><li>• Added the 32 mg cohort to the study.</li><li>• Changed the washout period after a single-dose to 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></ul>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

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

Notes: