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

Summary

EudraCT number	2016-005095-10
Trial protocol	GB DK FR DE
Global end of trial date	11 May 2021

Results information

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

Trial information

Trial identification

Sponsor protocol code	WVE-HDSNP1-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03225833
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Wave Life Sciences UK Limited
Sponsor organisation address	1 Chamberlain Square CS, Birmingham, United Kingdom, B3 3AX
Public contact	Chief Medical Officer, Wave Life Sciences, +1 617-949-2900, info@wavelifesci.com
Scientific contact	Chief Medical Officer, Wave Life Sciences, +1 617-949-2900, info@wavelifesci.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 May 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 May 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of WVE-120101 in patients with early manifest Huntington's disease (HD).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 December 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

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

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	60
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details:

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

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pooled Placebo

Arm description:

Placebo: 0.9% Sodium Chloride.

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

Dosage and administration details:

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

Arm title	WVE-120101 (2 milligram [mg])

Arm description:

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

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

Dosage and administration details:

WVE-120101 2 mg administered via intrathecal injection on Day 1 in single-dose phase followed by once every 4 weeks for a period of 8 weeks in multiple-dose phase.

Arm title	WVE-120101 (4 mg)

Arm description:

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

Arm type	Experimental

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

Dosage and administration details:

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

Arm title	WVE-120101 (8 mg)

Arm description:

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

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

Dosage and administration details:

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

Arm title	WVE-120101 (16 mg)

Arm description:

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

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

Dosage and administration details:

WVE-120101 16 mg administered via intrathecal injection on Day 1 in single-dose phase followed by once every 4 weeks for a period of 8 weeks in multiple-dose phase.

Arm title	WVE-120101 (32 mg)

Arm description:

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

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

Dosage and administration details:

WVE-120101 32 mg administered via intrathecal injection on Day 1 in single-dose phase followed by once every 4 weeks for a period of 8 weeks in multiple-dose phase.

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

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

Notes:

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

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

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

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

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

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

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

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

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

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

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.
[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.
[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.
[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.
[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Patients treated in single dose period only, multiple dose period only and both single dose and multiple dose periods in each reporting group are presented in separate milestones.

Baseline characteristics

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

Reporting group values	Pooled Placebo	WVE-120101 (2 milligram [mg])	WVE-120101 (4 mg)
Number of subjects	16	9	9
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	15	9	9
From 65-84 years	1	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	7	3	5
Male	9	6	4
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	16	9	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	16	9	9
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Australia	4	0	0
Canada	4	2	2
Denmark	0	0	0
France	1	0	0
Germany	2	0	0
Poland	4	7	5
United Kingdom	1	0	2
Diagnosis Stage Units: Subjects			
Stage 1	9	7	3
Stage 2	7	2	6
Time since initial diagnosis Units: years			
arithmetic mean	7	4.9	3.4
standard deviation	± 6.93	± 4.28	± 6.37
Age at Disease Onset Units: years			
arithmetic mean	40.75	37.33	42.89
standard deviation	± 11.079	± 7.826	± 9.280

Reporting group values	WVE-120101 (8 mg)	WVE-120101 (16 mg)	WVE-120101 (32 mg)
Number of subjects	9	8	10
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	9	8	10
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	6	1	7
Male	3	7	3
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	9	8	10

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

Reporting group values	Total		
Number of subjects	61		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	60		
From 65-84 years	1		
85 years and over	0		
Gender categorical Units: Subjects			
Female	29		
Male	32		

Ethnicity Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	61		
Unknown or Not Reported	0		
Race Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	61		
More than one race	0		
Unknown or Not Reported	0		
Region of Enrollment Units: Subjects			
Australia	17		
Canada	12		
Denmark	2		
France	4		
Germany	4		
Poland	19		
United Kingdom	3		
Diagnosis Stage Units: Subjects			
Stage 1	33		
Stage 2	28		
Time since initial diagnosis Units: years			
arithmetic mean			
standard deviation	-		
Age at Disease Onset Units: years			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

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

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

End point title	Safety: Number of Patients With Treatment-emergent Adverse Events (TEAEs)[1]

End point description:

All TEAEs reported or observed during the study, including TEAEs resulting from concurrent illnesses, reactions to concurrent medications, or progression of disease states. Safety population included all patients who received at least 1 dose of WVE-120101 or placebo. A summary of serious and all other non-serious adverse events (AEs), regardless of causality, is located in the reported AEs module.

End point type	Primary

End point timeframe:

Day 1 to end of study (up to Day 182 [32 mg cohort]/ Day 210 [all other cohorts])

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary end point.

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

End point values	WVE-120101 (16 mg)	WVE-120101 (32 mg)		

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

Statistical analyses

No statistical analyses for this end point

Primary: Safety: Number of Patients With Severe TEAEs

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

End point description:

Severity was evaluated using the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0. Safety population included all patients who received at least 1 dose of WVE-120101 or placebo. A summary of serious and all other non-serious AEs, regardless of causality, is located in the reported AEs module.

End point type	Primary

End point timeframe:

Day 1 to end of study (up to Day 182 [32 mg cohort]/ Day 210 [all other cohorts])

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary end point.

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

End point values	WVE-120101 (16 mg)	WVE-120101 (32 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	10		
Units: patients	0	5		

Statistical analyses

No statistical analyses for this end point

Primary: Safety: Number of Patients With Serious TEAEs

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

End point description:

A serious TEAE is defined as any event that results in death, is immediately life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect not present at prescreening. Safety population included all patients who received at least 1 dose of WVE-120101 or placebo. A summary of

serious and all other non-serious AEs, regardless of causality, is located in the reported AEs module.

End point type	Primary

End point timeframe:

Day 1 to end of study (up to Day 182 [32 mg cohort]/ Day 210 [all other cohorts])

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary end point.

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Patients withdraw from the study when serious or intolerable AE that in the Investigator’s opinion was reported. Safety population included all patients who received at least 1 dose of WVE-120101 or placebo. A summary of serious and all other non-serious AEs, regardless of causality, is located in the reported AEs module.

End point type	Primary

End point timeframe:

Day 1 to end of study (up to Day 182 [32 mg cohort]/ Day 210 [all other cohorts])

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary end point.

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

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

Statistical analyses

No statistical analyses for this end point

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

End point title	Pharmacokinetics (PK): Maximum Observed Concentration (Cmax)[5]

End point description:

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

End point type	Secondary

End point timeframe:

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

Notes:

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

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

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

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

Statistical analyses

No statistical analyses for this end point

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

End point title	PK: Time of Occurrence of Cmax (Tmax)[6]

End point description:

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

End point type	Secondary

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

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

Notes:

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

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

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

End point description:

Elimination rate of WVE-120101 from plasma (t1/2). The PK population included all treated patients in the safety population with at least 1 post-dose plasma or CSF WVE-120101 concentration measurement.

End point type	Secondary

End point timeframe:

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

Notes:

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

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

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

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

End point values	WVE-120101 (16 mg)	WVE-120101 (32 mg)		

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 to end of study (Day 182 [32 mg cohort in all regions except Canada] or Day 196 [32 mg cohort in Canada] or Day 210 [all other cohorts]).	
Adverse event reporting additional description:	
Safety population included all patients who received at least 1 dose of WVE-120101 or placebo.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	8.2

Reporting groups	
Reporting group title	Pooled Placebo
Reporting group description:	
Placebo: 0.9% Sodium Chloride.	
Reporting group title	WVE-120101 (2 mg)
Reporting group description:	
WVE-120101: WVE-120101 is a stereopure ASO.	
Reporting group title	WVE-120101 (4 mg)
Reporting group description:	
WVE-120101: WVE-120101 is a stereopure ASO.	
Reporting group title	WVE-120101 (8 mg)
Reporting group description:	
WVE-120101: WVE-120101 is a stereopure ASO.	
Reporting group title	WVE-120101 (16 mg)
Reporting group description:	
WVE-120101: WVE-120101 is a stereopure ASO.	
Reporting group title	WVE-120101 (32 mg)
Reporting group description:	
WVE-120101: WVE-120101 is a stereopure ASO.	

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

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

subjects affected / exposed	0 / 16 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disorientation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Non-serious adverse events	WVE-120101 (8 mg)	WVE-120101 (16 mg)	WVE-120101 (32 mg)

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

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

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

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

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

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

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

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 August 2018	• Implemented edits made in United Kingdom versions 0.1 and 0.2, and made minor clarifications and corrections. • Allowed patients to enter directly into the multiple-dose portion of the study. A separate schedule of assessments was added for these patients. • Added objective criteria for individual stopping criteria in the multiple-dose phase per Regulatory feedback. • Extended the washout required for other investigational agents to a minimum of 1 year.
21 January 2020	• Added the 32 mg cohort to the study. • For the 32 mg cohort, the washout period after a single dose was 4 weeks (instead of 8 weeks) based on available nonclinical and clinical data to date. A new schedule of assessments specific to the 32 mg cohort was added to account for this. • Change in the inclusion criterion for body mass index (ie, <=30 changed to <=32). • Addition of new urine sample PK assessments. • New electrocardiogram data collection timepoints.

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 treatment or dose escalation.

Notes: