



Clinical trial results:

A Multicenter, Randomized, Double-blind, Placebo-controlled, Phase 1b/2a Study of WVE-004 Administered Intrathecally to Patients with C9orf72-associated Amyotrophic Lateral Sclerosis (ALS) or Frontotemporal Dementia (FTD)

Summary

EudraCT number	2020-005193-94
Trial protocol	DE NL IE SE BE
Global end of trial date	27 June 2023

Results information

Result version number	v1 (current)
This version publication date	18 April 2025
First version publication date	18 April 2025

Trial information

Trial identification

Sponsor protocol code	WVE-004-001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04931862
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	Daniel Paulson, Wave Life Sciences, +1 617-949-2900, info@wavelifesci.com
Scientific contact	Daniel Paulson, 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	27 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 June 2023
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-004 in participants with amyotrophic lateral sclerosis (ALS) or frontotemporal dementia (FTD) with a documented mutation in the C9orf72 gene.

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	24 June 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Ireland: 3
Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	United Kingdom: 10
Worldwide total number of subjects	35
EEA total number of subjects	15

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)	25
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase 1b/2a randomized, double-blind, placebo-controlled study was conducted in adult participants with C9orf72-associated ALS or FTD at 14 investigational sites in 7 countries between 24 June 2021 and 27 June 2023. A total of 35 unique participants were enrolled in this study.

Pre-assignment

Screening details:

The study included 2 distinct periods: Period 1 (SAD) and Period 2 (MAD). A total of 23 participants were randomized to Period 1 and 21 participants (9 participants from Period 1 and 12 new participants) were randomized to Period 2.

Period 1

Period 1 title	SAD 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	SAD: Pooled Placebo

Arm description:

Participants were randomized to receive a single dose of placebo matching with WVE-004 on Day 1.

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:

Single dose of placebo matching with WVE-004 was administered IT by direct lumbar injection using an atraumatic needle on Day 1.

Arm title	SAD: WVE-004 10 mg
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Arm description:

Participants were randomized to receive a single dose of WVE-004 10 milligram (mg) intrathecal (IT) injection on Day 1.

Arm type	Experimental
Investigational medicinal product name	WVE-004
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Single dose of WVE-004 10 mg was administered IT by direct lumbar injection using an atraumatic needle on Day 1.

Arm title	SAD: WVE-004 20 mg
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Arm description:

Participants were randomized to receive a single dose of WVE-004 20 mg IT injection on Day 1.

Arm type	Experimental
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Investigational medicinal product name	WVE-004
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Single dose of WVE-004 20 mg was administered IT by direct lumbar injection using an atraumatic needle on Day 1.

Arm title	SAD: WVE-004 30 mg
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Arm description:

Participants were randomized to receive a single dose of WVE-004 30 mg IT injection on Day 1.

Arm type	Experimental
Investigational medicinal product name	WVE-004
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Single dose of WVE-004 30 mg was administered IT by direct lumbar injection using an atraumatic needle on Day 1.

Arm title	SAD: WVE-004 60 mg
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Arm description:

Participants were randomized to receive a single dose of WVE-004 60 mg IT injection on Day 1.

Arm type	Experimental
Investigational medicinal product name	WVE-004
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Single dose of WVE-004 60 mg was administered IT by direct lumbar injection using an atraumatic needle on Day 1.

Number of subjects in period 1^[1]	SAD: Pooled Placebo	SAD: WVE-004 10 mg	SAD: WVE-004 20 mg
Started	5	2	8
Treated	5	2	8
Completed	5	2	6
Not completed	0	0	2
Study terminated by Sponsor	-	-	1
Adverse event, non-fatal	-	-	-
Death	-	-	1

Number of subjects in period 1^[1]	SAD: WVE-004 30 mg	SAD: WVE-004 60 mg
Started	5	3

Treated	5	3
Completed	3	2
Not completed	2	1
Study terminated by Sponsor	-	-
Adverse event, non-fatal	1	1
Death	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: In addition to eligible participants from SAD period, newly enrolled participants were randomized into MAD period.

Period 2

Period 2 title	MAD Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	MAD: Pooled Placebo

Arm description:

Eligible participants from Period 1 and newly enrolled participants were randomized to receive placebo matching with WVE-004 once Q4W or Q12W for 12 weeks.

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-004 was administered IT by direct lumbar injection using an atraumatic needle Q4W or Q12W for 12 weeks.

Arm title	MAD: WVE-004 10 mg Q4W
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Arm description:

Eligible participants from Period 1 and newly enrolled participants were randomized to receive WVE-004 10 mg IT injection once Q4W for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	WVE-004
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

WVE-004 10 mg was administered IT by direct lumbar injection using an atraumatic needle Q4W for 12 weeks.

Arm title	MAD: WVE-004 10 mg Q12W
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Arm description:

Eligible participants from Period 1 and newly enrolled participants were randomized to receive WVE-004 10 mg IT injection once Q12W for 12 weeks.

Arm type	Experimental
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Investigational medicinal product name	WVE-004
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

WVE-004 10 mg was administered IT by direct lumbar injection using an atraumatic needle Q12W for 12 weeks.

Number of subjects in period 2^[2][3]	MAD: Pooled Placebo	MAD: WVE-004 10 mg Q4W	MAD: WVE-004 10 mg Q12W
Started	4	2	6
Treated	7	5	9
Completed	6	2	6
Not completed	1	4	3
Consent withdrawn by subject	1	1	1
Study terminated by Sponsor	-	-	1
Death	-	1	1
Unspecified	-	2	-
Joined	3	4	3
Transferred in from other group/arm	3	4	3

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: In addition to eligible participants from SAD period, newly enrolled participants were randomized into MAD period.

[3] - The number of subjects transferring in and out of the arms in the period are not the same. It is expected the net number of transfers in and out of the arms in a period, will be zero.

Justification: Newly enrolled participants were randomized directly into MAD period.

Baseline characteristics

Reporting groups

Reporting group title	SAD: Pooled Placebo
Reporting group description:	
Participants were randomized to receive a single dose of placebo matching with WVE-004 on Day 1.	
Reporting group title	SAD: WVE-004 10 mg
Reporting group description:	
Participants were randomized to receive a single dose of WVE-004 10 milligram (mg) intrathecal (IT) injection on Day 1.	
Reporting group title	SAD: WVE-004 20 mg
Reporting group description:	
Participants were randomized to receive a single dose of WVE-004 20 mg IT injection on Day 1.	
Reporting group title	SAD: WVE-004 30 mg
Reporting group description:	
Participants were randomized to receive a single dose of WVE-004 30 mg IT injection on Day 1.	
Reporting group title	SAD: WVE-004 60 mg
Reporting group description:	
Participants were randomized to receive a single dose of WVE-004 60 mg IT injection on Day 1.	

Reporting group values	SAD: Pooled Placebo	SAD: WVE-004 10 mg	SAD: WVE-004 20 mg
Number of subjects	5	2	8
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	69.2	60.5	59.0
standard deviation	± 6.30	± 0.71	± 6.89
Gender categorical			
Units: Subjects			
Female	3	1	2
Male	2	1	6
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	5	2	8
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	1
Black or African American	0	0	0
White	4	2	7
More than one race	0	0	0
Unknown or Not Reported	1	0	0

Reporting group values	SAD: WVE-004 30 mg	SAD: WVE-004 60 mg	Total
Number of subjects	5	3	23
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	57.6 ± 7.09	58.7 ± 9.07	-
Gender categorical Units: Subjects			
Female	4	2	12
Male	1	1	11
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	5	3	23
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	1
Black or African American	0	0	0
White	4	2	19
More than one race	0	0	0
Unknown or Not Reported	1	1	3

End points

End points reporting groups

Reporting group title	SAD: Pooled Placebo
Reporting group description: Participants were randomized to receive a single dose of placebo matching with WVE-004 on Day 1.	
Reporting group title	SAD: WVE-004 10 mg
Reporting group description: Participants were randomized to receive a single dose of WVE-004 10 milligram (mg) intrathecal (IT) injection on Day 1.	
Reporting group title	SAD: WVE-004 20 mg
Reporting group description: Participants were randomized to receive a single dose of WVE-004 20 mg IT injection on Day 1.	
Reporting group title	SAD: WVE-004 30 mg
Reporting group description: Participants were randomized to receive a single dose of WVE-004 30 mg IT injection on Day 1.	
Reporting group title	SAD: WVE-004 60 mg
Reporting group description: Participants were randomized to receive a single dose of WVE-004 60 mg IT injection on Day 1.	
Reporting group title	MAD: Pooled Placebo
Reporting group description: Eligible participants from Period 1 and newly enrolled participants were randomized to receive placebo matching with WVE-004 once Q4W or Q12W for 12 weeks.	
Reporting group title	MAD: WVE-004 10 mg Q4W
Reporting group description: Eligible participants from Period 1 and newly enrolled participants were randomized to receive WVE-004 10 mg IT injection once Q4W for 12 weeks.	
Reporting group title	MAD: WVE-004 10 mg Q12W
Reporting group description: Eligible participants from Period 1 and newly enrolled participants were randomized to receive WVE-004 10 mg IT injection once Q12W for 12 weeks.	

Primary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Serious Treatment-Emergent Adverse Events and Withdrew Due to Adverse Events

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Serious Treatment-Emergent Adverse Events and Withdrew Due to Adverse Events ^[1]
End point description: An adverse event (AE) was defined as any untoward medical occurrence in a participant enrolled into this study regardless of its causal relationship to study treatment. A serious AE was 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. A TEAE was defined as any event not present before exposure to study treatment or any event already present that worsens in either intensity or frequency after exposure to study treatment. The Safety population included all participants who were randomized and received at least 1 dose of study treatment.	
End point type	Primary
End point timeframe: From the first dose of study treatment (Day 1) up to 51 weeks (Period 1 = 24 weeks of follow-up and Period 2 = 12 weeks of treatment followed by 15 weeks of follow-up)	

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	SAD: Pooled Placebo	SAD: WVE-004 10 mg	SAD: WVE-004 20 mg	SAD: WVE-004 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	2	8	5
Units: participants				
TEAEs	5	2	8	5
Serious TEAEs	1	0	1	3
Adverse event leading to study discontinuation	0	0	0	1

End point values	SAD: WVE-004 60 mg	MAD: Pooled Placebo	MAD: WVE-004 10 mg Q4W	MAD: WVE-004 10 mg Q12W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	7	5	9
Units: participants				
TEAEs	3	7	5	7
Serious TEAEs	1	3	2	2
Adverse event leading to study discontinuation	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of WVE-004 in Plasma

End point title	Concentration of WVE-004 in Plasma
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End point description:

Blood samples collected to determine the concentration of WVE-004 in plasma. The Safety population included all participants who were randomized and received at least 1 dose of study treatment. Here, n= number of participants analyzed at specific timepoints, 9999= no participants analyzed and 99999= Standard deviation is not applicable when only 1 participant was analyzed.

End point type	Secondary
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End point timeframe:

Pre-dose on Days 1, 29, 57, and 85; 0.5, 1, 2, 4, and 6 hours post-dose on Days 1 and 85, Days 2, 3, 15, 113, 141, and 169 post-dose

End point values	SAD: Pooled Placebo	SAD: WVE-004 10 mg	SAD: WVE-004 20 mg	SAD: WVE-004 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	2	8	5
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Pre-dose (Day 1) (n=5,2,8,5,3,7,5,9)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
0.5 hours post-dose on Day 1 (n=5,2,8,5,3,7,5,8)	0.000 (± 0.0000)	11.072 (± 7.0407)	24.015 (± 26.5618)	110.872 (± 210.0965)
1 hour post-dose on Day 1 (n=5,2,8,5,3,7,5,9)	0.000 (± 0.0000)	15.600 (± 0.5798)	37.983 (± 29.0999)	232.260 (± 290.6490)
2 hours post-dose on Day 1 (n=5,2,8,5,3,7,5,9)	0.000 (± 0.0000)	15.755 (± 7.2196)	53.901 (± 36.8846)	254.616 (± 329.1846)
4 hours post-dose on Day 1 (n=5,2,8,5,3,7,5,9)	0.000 (± 0.0000)	15.915 (± 3.4860)	58.559 (± 25.9130)	181.638 (± 212.0959)
6 hours post-dose on Day 1 (n=5,2,8,5,3,7,5,9)	0.000 (± 0.0000)	12.437 (± 3.5822)	72.855 (± 37.4893)	164.356 (± 115.9532)
24 hours post-dose on Day 1 (n=5,2,8,5,3,7,5,9)	0.000 (± 0.0000)	7.048 (± 3.2690)	48.229 (± 19.4029)	67.372 (± 26.1047)
Day 3 (n=2,1,0,2,1,0,0,0)	0.000 (± 0.0000)	4.657 (± 99999)	9999 (± 9999)	19.072 (± 21.7761)
Day 15 (n=5,2,8,5,2,7,5,9)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.151 (± 0.2804)	0.786 (± 0.1557)
Day 29 (n=5,2,8,5,2,6,5,8)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.254 (± 0.3509)
Day 57 (n=5,2,7,4,3,7,5,9)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Day 85 (n=5,2,7,3,2,7,5,8)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
0.5 hours post-dose on Day 85 (n=0,0,0,0,0,6,5,8)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
1 hour post-dose on Day 85 (n=0,0,0,0,0,6,5,8)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
2 hours post-dose on Day 85 (n=0,0,0,0,0,6,5,8)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
4 hours post-dose on Day 85 (n=0,0,0,0,0,6,5,8)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
6 hours post-dose on Day 85 (n=0,0,0,0,0,6,4,8)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Day 113 (n=0,0,0,0,0,6,3,8)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Day 141 (n=0,0,0,0,0,6,2,7)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Day 169 (n=0,0,1,0,0,6,2,6)	9999 (± 9999)	9999 (± 9999)	0.000 (± 99999)	9999 (± 9999)
Pre-dose (Period 2 Day 1) (n=3,2,3,0,1,0,0,0)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	9999 (± 9999)

End point values	SAD: WVE-004 60 mg	MAD: Pooled Placebo	MAD: WVE-004 10 mg Q4W	MAD: WVE-004 10 mg Q12W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	7	5	9
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Pre-dose (Day 1) (n=5,2,8,5,3,7,5,9)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
0.5 hours post-dose on Day 1 (n=5,2,8,5,3,7,5,8)	982.573 (± 1576.5449)	0.000 (± 0.0000)	25.595 (± 41.3207)	12.811 (± 16.1575)

1 hour post-dose on Day 1 (n=5,2,8,5,3,7,5,9)	1566.820 (± 2535.1732)	0.000 (± 0.0000)	49.456 (± 79.2287)	39.632 (± 42.1030)
2 hours post-dose on Day 1 (n=5,2,8,5,3,7,5,9)	1153.337 (± 1810.6330)	0.000 (± 0.0000)	54.334 (± 89.6615)	62.059 (± 61.8641)
4 hours post-dose on Day 1 (n=5,2,8,5,3,7,5,9)	477.957 (± 604.5136)	0.000 (± 0.0000)	47.821 (± 68.9649)	68.896 (± 61.2281)
6 hours post-dose on Day 1 (n=5,2,8,5,3,7,5,9)	181.480 (± 123.6849)	0.000 (± 0.0000)	42.810 (± 42.9880)	50.609 (± 33.8274)
24 hours post-dose on Day 1 (n=5,2,8,5,3,7,5,9)	92.537 (± 66.2866)	0.000 (± 0.0000)	12.432 (± 4.4660)	26.894 (± 23.5717)
Day 3 (n=2,1,0,2,1,0,0,0)	5.201 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Day 15 (n=5,2,8,5,2,7,5,9)	0.693 (± 0.0472)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Day 29 (n=5,2,8,5,2,6,5,8)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Day 57 (n=5,2,7,4,3,7,5,9)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Day 85 (n=5,2,7,3,2,7,5,8)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
0.5 hours post-dose on Day 85 (n=0,0,0,0,0,6,5,8)	9999 (± 9999)	0.000 (± 0.0000)	21.729 (± 35.0917)	16.487 (± 16.0989)
1 hour post-dose on Day 85 (n=0,0,0,0,0,6,5,8)	9999 (± 9999)	0.000 (± 0.0000)	44.126 (± 69.8988)	47.824 (± 50.8331)
2 hours post-dose on Day 85 (n=0,0,0,0,0,6,5,8)	9999 (± 9999)	0.000 (± 0.0000)	41.473 (± 50.6066)	75.401 (± 73.2937)
4 hours post-dose on Day 85 (n=0,0,0,0,0,6,5,8)	9999 (± 9999)	0.000 (± 0.0000)	55.927 (± 66.4905)	82.305 (± 80.8516)
6 hours post-dose on Day 85 (n=0,0,0,0,0,6,4,8)	9999 (± 9999)	0.000 (± 0.0000)	31.173 (± 21.3997)	64.645 (± 52.1281)
Day 113 (n=0,0,0,0,0,6,3,8)	9999 (± 9999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Day 141 (n=0,0,0,0,0,6,2,7)	9999 (± 9999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Day 169 (n=0,0,1,0,0,6,2,6)	9999 (± 9999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Pre-dose (Period 2 Day 1) (n=3,2,3,0,1,0,0,0)	0.000 (± 0.0000)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of WVE-004 in Cerebrospinal Fluid (CSF)

End point title	Concentration of WVE-004 in Cerebrospinal Fluid (CSF)
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End point description:

CSF samples collected to determine the concentration of WVE-004 in CSF. The Safety population included all participants who were randomized and received at least 1 dose of study treatment. Here, n= number of participants analyzed at specific timepoints, 9999= no participants analyzed and 99999= Standard deviation is not applicable when only 1 participant was analyzed.

End point type	Secondary
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End point timeframe:

Period 1: Pre-dose; Days 15, 29, 57, 85, 113, 141 and 169; Period 2: Pre-dose; Days 29, 57, 85, 113, 141 and 169

End point values	SAD: Pooled Placebo	SAD: WVE-004 10 mg	SAD: WVE-004 20 mg	SAD: WVE-004 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	2	8	5
Units: ng/mL				
arithmetic mean (standard deviation)				
Pre-dose (n=5,2,8,5,3,7,5,9)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Day 15 (n=4,2,5,5,2,0,0,0)	0.000 (± 0.0000)	5.744 (± 1.1434)	15.070 (± 9.0216)	11.232 (± 3.2655)
Day 29 (n=5,1,8,5,3,5,5,8)	0.000 (± 0.0000)	4.689 (± 99999)	7.366 (± 2.3799)	5.921 (± 2.6947)
Day 57 (n=5,2,8,3,3,6,5,8)	0.000 (± 0.0000)	1.503 (± 2.1256)	3.894 (± 1.2476)	2.751 (± 1.6672)
Day 85 (n=5,2,7,3,2,6,5,8)	0.000 (± 0.0000)	0.985 (± 1.3923)	3.120 (± 1.5190)	1.863 (± 1.1513)
Day 113 (n=1,0,6,0,0,6,3,7)	0.000 (± 99999)	9999 (± 9999)	3.243 (± 2.1831)	9999 (± 9999)
Day 141 (n=1,0,4,0,0,4,2,6)	0.000 (± 99999)	9999 (± 9999)	2.198 (± 1.6976)	9999 (± 9999)
Day 169 (n=1,0,5,0,0,5,2,6)	0.000 (± 99999)	9999 (± 9999)	1.810 (± 1.2271)	9999 (± 9999)
Pre-dose (Period 2 Day 1) (n=3,2,3,0,1,0,0,0)	0.000 (± 0.0000)	0.000 (± 0.0000)	1.066 (± 1.1622)	9999 (± 9999)

End point values	SAD: WVE-004 60 mg	MAD: Pooled Placebo	MAD: WVE-004 10 mg Q4W	MAD: WVE-004 10 mg Q12W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	7	5	9
Units: ng/mL				
arithmetic mean (standard deviation)				
Pre-dose (n=5,2,8,5,3,7,5,9)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.355 (± 0.7885)
Day 15 (n=4,2,5,5,2,0,0,0)	11.024 (± 13.4584)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Day 29 (n=5,1,8,5,3,5,5,8)	7.234 (± 4.6744)	0.000 (± 0.0000)	4.047 (± 1.7556)	4.113 (± 1.4139)
Day 57 (n=5,2,8,3,3,6,5,8)	3.560 (± 3.1008)	0.000 (± 0.0000)	4.986 (± 1.9157)	2.953 (± 1.5480)
Day 85 (n=5,2,7,3,2,6,5,8)	2.283 (± 3.2286)	0.000 (± 0.0000)	5.299 (± 2.2021)	2.525 (± 1.6642)
Day 113 (n=1,0,6,0,0,6,3,7)	9999 (± 9999)	0.000 (± 0.0000)	7.825 (± 3.2123)	7.780 (± 3.5932)
Day 141 (n=1,0,4,0,0,4,2,6)	9999 (± 9999)	0.000 (± 0.0000)	4.236 (± 0.5006)	5.003 (± 2.0149)
Day 169 (n=1,0,5,0,0,5,2,6)	9999 (± 9999)	0.000 (± 0.0000)	3.816 (± 1.7444)	3.638 (± 1.7227)
Pre-dose (Period 2 Day 1) (n=3,2,3,0,1,0,0,0)	0.000 (± 0.0000)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Concentration of Poly Glycine-Proline (Poly-GP) Levels in the CSF Through Day 169

End point title	Change From Baseline in Concentration of Poly Glycine-Proline (Poly-GP) Levels in the CSF Through Day 169
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End point description:

CSF samples collected to determine the concentration of poly-GP levels in CSF. The Safety population included all participants who were randomized and received at least 1 dose of study treatment. Here, n= number of participants analyzed at specific timepoints, 9999= no participants analyzed and 99999= Standard deviation is not applicable when only 1 participant was analyzed.

End point type	Secondary
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End point timeframe:

Period 1: Baseline (Day 1) and Days 15, 29, 57, 85, 113, 141 and 169; Period 2: Baseline (Day 1) and Days 29, 57, 85, 113, 141, and 169

End point values	SAD: Pooled Placebo	SAD: WVE-004 10 mg	SAD: WVE-004 20 mg	SAD: WVE-004 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	2	8	5
Units: picogram/mL				
arithmetic mean (standard deviation)				
Baseline (Day 1) (n=5,2,8,5,3,7,5,9)	28.03 (± 19.943)	140.80 (± 158.675)	15.88 (± 4.165)	21.23 (± 10.820)
Day 15 (n=4,2,5,5,2,0,0,0)	25.74 (± 23.325)	133.80 (± 137.462)	12.86 (± 6.504)	15.67 (± 10.217)
Day 29 (n=5,1,8,5,3,5,5,8)	29.21 (± 20.874)	238.00 (± 99999)	13.57 (± 4.759)	14.23 (± 10.075)
Day 57 (n=5,2,8,3,3,6,5,8)	28.99 (± 21.130)	111.05 (± 124.380)	10.88 (± 4.111)	14.27 (± 7.419)
Day 85 (n=5,2,7,3,2,6,5,8)	29.49 (± 20.546)	116.75 (± 109.248)	11.01 (± 3.117)	11.92 (± 4.175)
Day 113 (n=1,0,6,0,0,6,3,7)	44.70 (± 99999)	9999 (± 9999)	10.13 (± 3.524)	9999 (± 9999)
Day 141 (n=1,0,4,0,0,4,2,6)	40.60 (± 99999)	9999 (± 9999)	10.49 (± 3.241)	9999 (± 9999)
Day 169 (n=1,0,5,0,0,5,2,6)	44.60 (± 99999)	9999 (± 9999)	9.06 (± 3.544)	9999 (± 9999)
Period 2 Day 1 (n=3,2,3,0,1,0,0,0)	15.98 (± 12.452)	116.15 (± 111.511)	8.19 (± 3.815)	9999 (± 9999)

End point values	SAD: WVE-004 60 mg	MAD: Pooled Placebo	MAD: WVE-004 10 mg Q4W	MAD: WVE-004 10 mg Q12W
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Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	7	5	9
Units: picogram/mL				
arithmetic mean (standard deviation)				
Baseline (Day 1) (n=5,2,8,5,3,7,5,9)	32.97 (± 9.581)	21.69 (± 9.896)	60.84 (± 76.321)	20.70 (± 19.759)
Day 15 (n=4,2,5,5,2,0,0,0)	29.65 (± 14.071)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Day 29 (n=5,1,8,5,3,5,5,8)	28.93 (± 6.824)	20.67 (± 12.253)	53.50 (± 66.685)	17.85 (± 12.840)
Day 57 (n=5,2,8,3,3,6,5,8)	22.83 (± 5.934)	19.89 (± 9.813)	47.99 (± 57.109)	16.76 (± 12.696)
Day 85 (n=5,2,7,3,2,6,5,8)	25.15 (± 7.425)	19.39 (± 10.713)	46.51 (± 53.808)	17.06 (± 12.298)
Day 113 (n=1,0,6,0,0,6,3,7)	9999 (± 9999)	18.71 (± 9.423)	17.40 (± 12.025)	12.35 (± 10.967)
Day 141 (n=1,0,4,0,0,4,2,6)	9999 (± 9999)	20.21 (± 12.370)	54.10 (± 38.184)	13.75 (± 12.458)
Day 169 (n=1,0,5,0,0,5,2,6)	9999 (± 9999)	21.27 (± 11.246)	48.35 (± 29.911)	14.88 (± 15.261)
Period 2 Day 1 (n=3,2,3,0,1,0,0,0)	19.30 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TEAEs were collected from the first dose of study treatment (Day 1) up to 51 weeks (Period 1 = 24 weeks of follow-up and Period 2 = 12 weeks of treatment followed by 15 weeks of follow-up)

Adverse event reporting additional description:

The Safety population included all participants who were randomized and received at least 1 dose of study treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.0
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Reporting groups

Reporting group title	SAD: Pooled Placebo
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Reporting group description:

Participants were randomized to receive a single dose of placebo matching with WVE-004 on Day 1.

Reporting group title	SAD: WVE-004 10 mg
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Reporting group description:

Participants were randomized to receive a single dose of WVE-004 10 mg IT injection on Day 1.

Reporting group title	SAD: WVE-004 20 mg
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Reporting group description:

Participants were randomized to receive a single dose of WVE-004 20 mg IT injection on Day 1.

Reporting group title	SAD: WVE-004 30 mg
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Reporting group description:

Participants were randomized to receive a single dose of WVE-004 30 mg IT injection on Day 1.

Reporting group title	SAD: WVE-004 60 mg
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Reporting group description:

Participants were randomized to receive a single dose of WVE-004 60 mg IT injection on Day 1.

Reporting group title	MAD: Pooled Placebo
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Reporting group description:

Eligible participants from Period 1 and newly enrolled participants were randomized to receive placebo matching with WVE-004 Q4W or Q12W for 12 weeks.

Reporting group title	MAD: WVE-004 10 mg Q4W
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Reporting group description:

Eligible participants from Period 1 and newly enrolled participants were randomized to receive WVE-004 10 mg IT injection Q4W for 12 weeks.

Reporting group title	MAD: WVE-004 10 mg Q12W
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Reporting group description:

Eligible participants from Period 1 and newly enrolled participants were randomized to receive WVE-004 10 mg IT injection Q12W for 12 weeks.

Serious adverse events	SAD: Pooled Placebo	SAD: WVE-004 10 mg	SAD: WVE-004 20 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1

Investigations			
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (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			
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (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
Head injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (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
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (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			
Cerebellar syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (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
Sensory loss			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (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
Status epilepticus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (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			
Disease progression			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (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
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (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
Dysphagia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 8 (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
Respiratory failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (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			
Delirium			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (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			
Pneumonia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (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
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (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	SAD: WVE-004 30 mg	SAD: WVE-004 60 mg	MAD: Pooled Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)	1 / 3 (33.33%)	3 / 7 (42.86%)
number of deaths (all causes)	2	1	0
number of deaths resulting from adverse events	2	1	0
Investigations			
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (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			
Fall			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 7 (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
Head injury			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 7 (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
Post lumbar puncture syndrome			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 7 (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
Nervous system disorders			
Cerebellar syndrome			

subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Sensory loss			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (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			
Disease progression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (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
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			

subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (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
Respiratory failure			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (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
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (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	MAD: WVE-004 10 mg Q4W	MAD: WVE-004 10 mg Q12W	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	2 / 9 (22.22%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	1	
Investigations			
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebellar syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sensory loss			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	2 / 5 (40.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 5 (40.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	SAD: Pooled Placebo	SAD: WVE-004 10 mg	SAD: WVE-004 20 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	2 / 2 (100.00%)	8 / 8 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Peripheral coldness			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 5 (20.00%)	1 / 2 (50.00%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Feeling cold			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Injection site discomfort subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Medical device site pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Choking subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Lung consolidation subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Lung disorder subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Respiratory failure subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Psychiatric disorders Delirium subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	2 / 8 (25.00%) 2

Poor quality sleep subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Suicidal ideation subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Product issues Device physical property issue subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Investigations Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Blood fibrinogen decreased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Blood urine present subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Body temperature increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
C-reactive protein increased subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Coagulation test abnormal subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Glycosylated haemoglobin increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Heart rate increased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Administration related reaction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bone contusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Concussion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Fall			
subjects affected / exposed	1 / 5 (20.00%)	1 / 2 (50.00%)	3 / 8 (37.50%)
occurrences (all)	1	1	3
Head injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Post lumbar puncture syndrome			
subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	2 / 8 (25.00%)
occurrences (all)	2	0	2
Procedural pain			

subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	3 / 8 (37.50%)
occurrences (all)	2	0	3
Scratch			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Skin laceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Soft tissue injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Stoma site hypergranulation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cerebellar syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dizziness			

subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	4 / 5 (80.00%)	0 / 2 (0.00%)	5 / 8 (62.50%)
occurrences (all)	4	0	5
Hypoaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
IIIrd nerve disorder			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Loss of consciousness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscle contractions involuntary			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Polyneuropathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Sciatica			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Sensory loss			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Status epilepticus			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Taste disorder subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Leukocytosis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Eye disorders Eye movement disorder subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Periorbital oedema subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Vision blurred subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Abdominal pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Constipation			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Dysphagia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	2 / 8 (25.00%)
occurrences (all)	0	1	2
Oral discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dermatitis exfoliative			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Drug eruption			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nail discolouration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hypertonic bladder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Leukocyturia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Proteinuria			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	3 / 8 (37.50%)
occurrences (all)	1	0	3
Flank pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	2	0	1
Muscle twitching			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Myalgia			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Neck pain subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Periarthritis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Infections and infestations			
Asymptomatic bacteriuria subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Bacteriuria subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
COVID-19 subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	2 / 8 (25.00%) 2
Chlamydial infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Herpes simplex subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Hordeolum subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Laryngitis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1

Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	SAD: WVE-004 30 mg	SAD: WVE-004 60 mg	MAD: Pooled Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	3 / 3 (100.00%)	7 / 7 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of skin			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Haematoma			

subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Peripheral coldness			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	2 / 5 (40.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Fatigue			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	2
Feeling cold			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Feeling hot			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injection site discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Medical device site pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			

Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1	0 / 7 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Choking subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Lung consolidation subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Lung disorder subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Respiratory failure subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Psychiatric disorders			
Delirium subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1	0 / 7 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Poor quality sleep subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Suicidal ideation subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Product issues			
Device physical property issue subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0

Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Blood fibrinogen decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Blood urine present			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Coagulation test abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Administration related reaction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Bone contusion			

subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Concussion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	1 / 5 (20.00%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
Head injury			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Infusion related reaction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Post lumbar puncture syndrome			
subjects affected / exposed	2 / 5 (40.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Procedural pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Skin laceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Soft tissue injury			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Stoma site hypergranulation subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Wound subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Nervous system disorders Balance disorder subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Cerebellar syndrome subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1	0 / 7 (0.00%) 0
Cognitive disorder subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Headache subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 3 (33.33%) 1	3 / 7 (42.86%) 3
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	2 / 7 (28.57%) 2
IIIrd nerve disorder subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Loss of consciousness			

subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Muscle contractions involuntary			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Sensory loss			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Status epilepticus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Leukocytosis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Eye disorders Eye movement disorder subjects affected / exposed occurrences (all) Periorbital oedema subjects affected / exposed occurrences (all) Vision blurred subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	1 / 7 (14.29%) 1 0 / 7 (0.00%) 0 1 / 7 (14.29%) 1
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dry mouth subjects affected / exposed occurrences (all) Dysphagia subjects affected / exposed occurrences (all) Frequent bowel movements	0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	0 / 7 (0.00%) 0 0 / 7 (0.00%) 0 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 0 / 7 (0.00%) 0

subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Oral discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Oral pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dermatitis exfoliative			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Drug eruption			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Nail discolouration subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Renal and urinary disorders			
Dysuria subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Glycosuria subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Haematuria subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Hypertonic bladder subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Leukocyturia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Pollakiuria subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Proteinuria subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Urinary incontinence subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1	0 / 7 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 3 (33.33%) 1	1 / 7 (14.29%) 1
Flank pain			

subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Muscle twitching			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	2 / 5 (40.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Periarthritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Bacteriuria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Chlamydial infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hordeolum			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	2
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dehydration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	MAD: WVE-004 10 mg Q4W	MAD: WVE-004 10 mg Q12W	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	7 / 9 (77.78%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Peripheral coldness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	3 / 5 (60.00%)	0 / 9 (0.00%)	
occurrences (all)	3	0	

Feeling cold subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Feeling hot subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	
Gait disturbance subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 9 (0.00%) 0	
Injection site discomfort subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 9 (0.00%) 0	
Medical device site pain subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 9 (0.00%) 0	
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Choking subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Cough subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Lung consolidation subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Lung disorder subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	
Respiratory failure			

subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2	1 / 9 (11.11%) 1	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Poor quality sleep			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Suicidal ideation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Product issues			
Device physical property issue			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Blood fibrinogen decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Blood urine present			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Body temperature increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
C-reactive protein increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Coagulation test abnormal			

subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Heart rate increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	2 / 5 (40.00%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Injury, poisoning and procedural complications			
Administration related reaction			
subjects affected / exposed	2 / 5 (40.00%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Bone contusion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Concussion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Contusion			
subjects affected / exposed	1 / 5 (20.00%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Fall			
subjects affected / exposed	4 / 5 (80.00%)	5 / 9 (55.56%)	
occurrences (all)	4	5	
Head injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Infusion related reaction			

subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Muscle strain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Post lumbar puncture syndrome			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	0 / 5 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
Scratch			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Skin abrasion			
subjects affected / exposed	1 / 5 (20.00%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Skin laceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Soft tissue injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Stoma site hypergranulation			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Wound			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Balance disorder			

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0
Cerebellar syndrome		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0
Cognitive disorder		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0
Dizziness		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0
Headache		
subjects affected / exposed	1 / 5 (20.00%)	2 / 9 (22.22%)
occurrences (all)	1	2
Hypoaesthesia		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	1
IIIrd nerve disorder		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0
Loss of consciousness		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0
Migraine		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0
Muscle contractions involuntary		
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)
occurrences (all)	1	0
Paraesthesia		
subjects affected / exposed	1 / 5 (20.00%)	1 / 9 (11.11%)
occurrences (all)	1	1
Polyneuropathy		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	1
Restless legs syndrome		

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Sciatica subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Sensory loss subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Status epilepticus subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	
Taste disorder subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	
Tremor subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Leukocytosis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Eye disorders Eye movement disorder subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Periorbital oedema subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 9 (0.00%) 0	
Vision blurred			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Dry mouth			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	2 / 5 (40.00%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Frequent bowel movements			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Oral discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Oral pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	

Vomiting subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Skin and subcutaneous tissue disorders			
Decubitus ulcer subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 9 (0.00%) 0	
Dermatitis exfoliative subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Drug eruption subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 9 (0.00%) 0	
Dry skin subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Eczema subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Erythema subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	
Nail discolouration subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	
Renal and urinary disorders			
Dysuria subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	
Glycosuria subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 9 (0.00%) 0	
Haematuria subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	
Hypertonic bladder			

subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Leukocyturia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Proteinuria			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Urinary incontinence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	2 / 5 (40.00%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Flank pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Muscle twitching			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	2 / 5 (40.00%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal chest pain			

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Neck pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Periarthritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Asymptomatic bacteriuria			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Bacteriuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
COVID-19			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Chlamydial infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Herpes simplex			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	

Hordeolum			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Laryngitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
Pneumonia			
subjects affected / exposed	2 / 5 (40.00%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Dehydration			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Hyponatraemia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Hypophosphataemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 December 2020	<ul style="list-style-type: none">• Removed National Cancer Institute Common Terminology Criteria for Adverse Events for AE categorization.• Removed optionality for pre-lumbar puncture (LP) prothrombin time and platelet testing at the Early Termination Visit in Period 1.
23 August 2021	<ul style="list-style-type: none">• Updated planned dosing regimen in Period 2 Cycle 1 based on available nonclinical Pharmacokinetic and toxicology data.• Revised randomization of new participants in Period 2 to ensure a balance of treatment and placebo participants within disease type.• Modified Period 2 and individual stopping criteria in accordance with regulatory feedback across multiple regions.• Revised to require all participants (not just FTD and mixed phenotype) perform Clinical Dementia Rating plus National Alzheimer's Coordinating Center Frontotemporal Lobar Degeneration at Screening.• Clarified data required for dose escalation decision.• Clarified timing and duration of contraception.
02 May 2022	<ul style="list-style-type: none">• Revised to allow additional participants from Period 1 to receive Period 2 Cycle 1 dose level based on available clinical data.• Provided further clarification regarding potential bleeding disorders that expose participants to risk of injury or unsuccessful LP.• Added exclusion criterion for antiplatelet or anticoagulant concomitant therapies, in accordance with Regulatory feedback.• Provided further clarity regarding the flexibility of the Dose Escalation Committee (DEC) and Data Safety Monitoring Board (DSMB) to change dose level and frequency.• Added additional visits and assessments to further assess Pharmacokinetic, Pharmacodynamic, safety, and clinical effects.• Aligned highly effective methods of contraception with regional regulatory feedback.
07 October 2022	<ul style="list-style-type: none">• Updated to indicate that the maximum dose level and frequency in Period 2 would not exceed 20 mg Q12W based on recommendations by the DEC/DSMB.• Added Protocol Section 2.4 to reflect the current status of the adaptive design allowing only participation in Period 1 and Period 2, or Period 2 only.• Added a digital health technology device to gain additional data on potential clinical effects of WVE-004.

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.

Due to lack of clinical benefit, development of WVE-004 was stopped.

Notes: