Clinical trial results:
A Randomized, Multicenter, Double-Blind, Placebo-Controlled, Phase III Clinical Study to Evaluate the Efficacy and Safety of Intrathecally Administered RO7234292 (RG6042) in Patients With Manifest Huntington's Disease

Summary

EudraCT number	2018-002987-14
Trial protocol	GB DK NL AT PL IT
Global end of trial date	17 March 2022

Results information

Result version number	v1 (current)
This version publication date	01 April 2023
First version publication date	01 April 2023

Trial information

Trial identification

Sponsor protocol code	BN40423

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, Roche Trial Information Hotline, +41 61 6878333,
Scientific contact	Medical Communications, Hoffmann-La Roche, +41 800 8218590, genentech@druginfo.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	09 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 March 2022
Global end of trial reached?	Yes
Global end of trial date	17 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

A Study to Evaluate the Efficacy and Safety of Intrathecally Administered RO7234292 (RG6042) in participants with Manifest Huntington's Disease

Protection of trial subjects:

The study was conducted in accordance with the principles of the “Declaration of Helsinki” and Good Clinical Practice (GCP) guidelines according to the regulations and procedures described in the protocol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 January 2019
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	Argentina: 34
Country: Number of subjects enrolled	Australia: 21
Country: Number of subjects enrolled	Austria: 27
Country: Number of subjects enrolled	Canada: 55
Country: Number of subjects enrolled	Switzerland: 21
Country: Number of subjects enrolled	Chile: 10
Country: Number of subjects enrolled	Germany: 87
Country: Number of subjects enrolled	Denmark: 18
Country: Number of subjects enrolled	Spain: 146
Country: Number of subjects enrolled	France: 69
Country: Number of subjects enrolled	United Kingdom: 46
Country: Number of subjects enrolled	Italy: 54
Country: Number of subjects enrolled	Japan: 10
Country: Number of subjects enrolled	Netherlands: 16
Country: Number of subjects enrolled	New Zealand: 19
Country: Number of subjects enrolled	Poland: 28
Country: Number of subjects enrolled	Russian Federation: 19
Country: Number of subjects enrolled	United States: 219
Worldwide total number of subjects	899
EEA total number of subjects	445

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)	888
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study BN40423 was originally designed including3 dosing regimens under a double-blinded monthly dosing paradigm: tominersen Q4W, tominersen every 8 weeks (Q8W) with alternating placebo, and placebo Q4W. The Sponsor decided to stop enrollment into the ODC and NDC started with new participants with 120mg tominersen Q8W and Q16W

Pre-assignment

Screening details:

The study has 2 parts: Original Design Cohorts (ODC) and New Design Cohorts. (NDH) Participants in the two parts' cohorts are separate and sequential.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo ODC

Arm description:

Matching Placebo Q4W

Arm type	Placebo
Investigational medicinal product name	Matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo for RO7234292 120 mg Q4W from Week 1 to Week 69

Arm title	RO7234292 Q4W ODC

Arm description:

RO7234292 120 mg Q4W

Arm type	Experimental
Investigational medicinal product name	Tominersen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

RO7234292 120 mg Q4W from Week 1 to Week 69

Arm title	RO7234292 Q8W ODC

Arm description:

RO7234292 120 mg Q8W

Arm type	Experimental

Investigational medicinal product name	Tominersen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

RO7234292 120 mg Q8W from Week 1 to Week 69

Arm title	Tomi 120 mg Q8W NDC

Arm description:

NDC Arms were enrolled after the completion of ODC

Arm type	Experimental
Investigational medicinal product name	Tominersen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Tomi 120 mg Q8W NDC

Arm title	Tomi 120mg Q16W NDC

Arm description:

NDC Arms were enrolled after the completion of ODC

Arm type	Experimental
Investigational medicinal product name	Tominersen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Tomi 120mg Q16W NDC

Arm title	Placebo NDC

Arm description:

NDC Arms were enrolled after the completion of ODC

Arm type	Placebo
Investigational medicinal product name	Tominersen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo NDC

Number of subjects in period 1	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC
Started	36	36	36
Completed	0	0	0
Not completed	36	36	36
Adverse event, serious fatal	-	-	-

Consent withdrawn by subject	-	-	-
Physician decision	-	-	-
Adverse event, non-fatal	-	1	-
did not visit	-	1	-
Participant could not come to site	-	-	-
transferred to OpenLabelExtension	35	33	36
Lost to follow-up	-	1	-
Repeated MRI dId not pass QC.	1	-	-
SF- safety Finding	-	-	-
Protocol deviation	-	-	-

Number of subjects in period 1	Tomi 120 mg Q8W NDC	Tomi 120mg Q16W NDC	Placebo NDC
Started	263	264	264
Completed	216	207	211
Not completed	47	57	53
Adverse event, serious fatal	1	1	3
Consent withdrawn by subject	41	43	35
Physician decision	1	4	4
Adverse event, non-fatal	-	2	3
did not visit	-	-	1
Participant could not come to site	-	1	-
transferred to OpenLabelExtension	-	-	-
Lost to follow-up	2	4	5
Repeated MRI dId not pass QC.	-	-	-
SF- safety Finding	-	-	1
Protocol deviation	2	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo ODC
Reporting group description:	
Matching Placebo Q4W	
Reporting group title	RO7234292 Q4W ODC
Reporting group description:	
RO7234292 120 mg Q4W	
Reporting group title	RO7234292 Q8W ODC
Reporting group description:	
RO7234292 120 mg Q8W	
Reporting group title	Tomi 120 mg Q8W NDC
Reporting group description:	
NDC Arms were enrolled after the completion of ODC	
Reporting group title	Tomi 120mg Q16W NDC
Reporting group description:	
NDC Arms were enrolled after the completion of ODC	
Reporting group title	Placebo NDC
Reporting group description:	
NDC Arms were enrolled after the completion of ODC	

Reporting group values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC
Number of subjects	36	36	36
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)	36	35	36
From 65-84 years	0	1	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	45.2	44.9	47.7
standard deviation	± 11.0	± 9.8	± 9.7
Sex: Female, Male Units: Participants			
Female	22	17	23
Male	14	19	13
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	0

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	0
White	33	36	36
More than one race	1	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	8	3	7
Not Hispanic or Latino	28	33	29
Unknown or Not Reported	0	0	0

Reporting group values	Tomi 120 mg Q8W NDC	Tomi 120mg Q16W NDC	Placebo NDC
Number of subjects	263	264	264
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)	258	261	262
From 65-84 years	5	3	2
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	47.8	47.5	48.7
standard deviation	± 9.6	± 9.3	± 9.9
Sex: Female, Male			
Units: Participants			
Female	112	130	114
Male	151	134	150
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1	2	0
Asian	5	4	3
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	0
White	249	248	250
More than one race	0	1	0
Unknown or Not Reported	7	8	11
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	34	38	30
Not Hispanic or Latino	225	218	226
Unknown or Not Reported	4	8	8

Reporting group values	Total		

Number of subjects	899		
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)	888		
From 65-84 years	11		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	418		
Male	481		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	3		
Asian	13		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	3		
White	852		
More than one race	2		
Unknown or Not Reported	26		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	120		
Not Hispanic or Latino	759		
Unknown or Not Reported	20		

End points

End points reporting groups

Reporting group title	Placebo ODC
Reporting group description: Matching Placebo Q4W	
Reporting group title	RO7234292 Q4W ODC
Reporting group description: RO7234292 120 mg Q4W	
Reporting group title	RO7234292 Q8W ODC
Reporting group description: RO7234292 120 mg Q8W	
Reporting group title	Tomi 120 mg Q8W NDC
Reporting group description: NDC Arms were enrolled after the completion of ODC	
Reporting group title	Tomi 120mg Q16W NDC
Reporting group description: NDC Arms were enrolled after the completion of ODC	
Reporting group title	Placebo NDC
Reporting group description: NDC Arms were enrolled after the completion of ODC	

Primary: Change from Baseline in the Composite Unified Huntington's Disease Rating Scale (cUHDRS)

End point title	Change from Baseline in the Composite Unified Huntington's Disease Rating Scale (cUHDRS)[1]
End point description: Original Design and New Design Cohorts are reported. 9999 values represents not evaluable data.	
End point type	Primary
End point timeframe: Weeks 21 and 69	

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 statistics was planned to be reported in the endpoint.

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	34	36	260
Units: Score on a Scale				
least squares mean (standard error)				
Week 21	0.103 (± 0.193)	-0.367 (± 0.189)	-0.139 (± 0.197)	9999 (± 9999)
Week 69	9999 (± 9999)	-0.367 (± 0.189)	9999 (± 9999)	-1.173 (± 0.091)

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	260		
Units: Score on a Scale				
least squares mean (standard error)				
Week 21	9999 (± 9999)	9999 (± 9999)		
Week 69	-0.793 (± 0.093)	-0.630 (± 0.091)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in the TFC Score

End point title	Change From Baseline in the TFC Score[2]
End point description:	
9999 represent no evaluable data	
End point type	Primary
End point timeframe:	
Weeks 21 and 69	

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 statistics was planned to be reported in the endpoint.

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35[3]	34	36	260
Units: Score on a scale				
least squares mean (standard error)				
Week 21	0.150 (± 0.246)	-0.463 (± 0.242)	-0.46 (± 0.255)	9999 (± 9999)
Week 69	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	-1.284 (± 0.124)

Notes:

[3] - No drug dosing

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	260[4]		
Units: Score on a scale				
least squares mean (standard error)				
Week 21	9999 (± 9999)	9999 (± 9999)		
Week 69	-0.921 (± 0.126)	-0.883 (± 0.124)		

Notes:

[4] - No drug dosing

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Motor Score (TMS)

End point title	Change From Baseline in Total Motor Score (TMS)
End point description: 9999 represent no evaluable data	
End point type	Secondary
End point timeframe: Weeks 21 and 69	

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	34	36	260
Units: Score on a Scale				
least squares mean (standard error)				
Week 21	-1.977 (± 1.407)	2.570 (± 0.542)	1.493 (± 0.78)	9999 (± 9999)
Week 69	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	4.028 (± 0.575)

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	260		
Units: Score on a Scale				
least squares mean (standard error)				
Week 21	9999 (± 9999)	9999 (± 9999)		
Week 69	3.524 (± 0.583)	3.513 (± 0.573)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Symbol Digit Modalities Test (SDMT)

End point title	Change From Baseline in Symbol Digit Modalities Test (SDMT)
End point description: 9999 represents no evaluable data	
End point type	Secondary
End point timeframe: Weeks 21 and 69	

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	36	260
Units: Score on a scale				
least squares mean (standard error)				
Week 21	1.865 (± 0.886)	-1.166 (± 0.867)	1.204 (± 0.879)	9999 (± 9999)
Week 69	9999 (± 9999)	-1.166 (± 0.867)	9999 (± 9999)	-2.641 (± 0.380)

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	260		
Units: Score on a scale				
least squares mean (standard error)				
Week 21	9999 (± 9999)	9999 (± 9999)		
Week 69	-0.996 (± 0.385)	-0.216 (± 0.379)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Clinical Global Impression, Severity Scale (CGI-S)

End point title	Change From Baseline in the Clinical Global Impression, Severity Scale (CGI-S)

End point description:

Only NDC Participants data are available and reported.

End point type	Secondary

End point timeframe:

Week 69

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[5]	0[6]	0[7]	260
Units: Scores on a Scale				
least squares mean (standard error)	()	()	()	0.662 (± 0.093)

Notes:
[5] - No subjects
[6] - No subjects
[7] - No subjects

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	260		
Units: Scores on a Scale				
least squares mean (standard error)	0.640 (± 0.094)	0.545 (± 0.093)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Stroop Word Reading (SWR) Test

End point title	Change From Baseline in Stroop Word Reading (SWR) Test

End point description:

End point type	Secondary

End point timeframe:
Weeks 21 and 69

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	36	258
Units: Score on a Scale				
least squares mean (standard error)				
Week 21	-1.397 (± 1.902)	0.469 (± 1.847)	-1.036 (± 1.842)	9999 (± 9999)
Week 69	9999 (± 9999)	0.469 (± 1.847)	9999 (± 9999)	-5.224 (± 0.803)

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	260		
Units: Score on a Scale				
least squares mean (standard error)				
Week 21	9999 (± 9999)	9999 (± 9999)		
Week 69	-3.949 (± 0.815)	-2.555 (± 0.802)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients with a Decrease From Baseline of >=1 point on the TFC

End point title	Percentage of Patients with a Decrease From Baseline of >=1 point on the TFC

End point description:

Only NDC participant data are available and reported

End point type	Secondary

End point timeframe:

Week 69

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[8]	0[9]	0[10]	260
Units: Percentage				
number (not applicable)				
Week 69 Yes				55.7
Week 69 No				44.3

Notes:

[8] - No subjects

[9] - No subjects

[10] - No Subjects

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	260		
Units: Percentage				
number (not applicable)				
Week 69 Yes	50.3	49.5		
Week 69 No	49.7	43.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With a Decline From Baseline of >=1.2 Points on

the cUHDRS

End point title	Percentage of Patients With a Decline From Baseline of >=1.2 Points on the cUHDRS

End point description:

Only NDC available.

End point type	Secondary

End point timeframe:

Up to Week 69

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[11]	0[12]	0[13]	260
Units: Percentage of Participants				
number (not applicable)				
Week 69 Yes				44.5
Week 69 No				55.5

Notes:

[11] - No subjects

[12] - No subjects

[13] - No subjects

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	260		
Units: Percentage of Participants				
number (not applicable)				
Week 69 Yes	32.1	29.7		
Week 69 No	67.9	70.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With an Unchanged or Improved Score on the Clinical Global Impression, Change Scale (CGI-C) Score

End point title	Percentage of Patients With an Unchanged or Improved Score on the Clinical Global Impression, Change Scale (CGI-C) Score

End point description:

End point type	Secondary

End point timeframe:

Weeks 53 and 69

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[14]	0[15]	0[16]	260
Units: Percentage				
number (not applicable)				
Week 53 Yes				38.1
Week 53 No				38.1
Week 69 Yes				55.4
Week 69 No				44.6

Notes:

[14] - No subjects

[15] - No subjects

[16] - No subjects

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	260		
Units: Percentage				
number (not applicable)				
Week 53 Yes	64.2	63.6		
Week 53 No	35.8	36.4		
Week 69 Yes	59.6	56.3		
Week 69 No	40.4	43.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Adverse Events

End point title	Percentage of Participants with Adverse Events

End point description:

End point type	Secondary

End point timeframe:

Up to 117 Weeks (29 months)

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	36	260
Units: Percentage				
number (not applicable)				
Total number of patients with at least one AE	77.8	80.0	61.1	13.1

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	260		
Units: Percentage				
number (not applicable)				
Total number of patients with at least one AE	8.0	9.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Montreal Cognitive Assessment (MoCA)

End point title	Change From Baseline in Montreal Cognitive Assessment (MoCA)

End point description:

ODC Week 21 and NDC Week 69 data were reportable.

9999 represents values not reportable

End point type	Secondary

End point timeframe:

Screening, Baseline, Weeks 5, 21, 37, 53, 69, 85 and 101 and early treatment termination

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	36	260
Units: Scores on a Sclae				
arithmetic mean (standard deviation)				
Week 21	-0.07 (± 0.86)	0.10 (± 1.37)	0.33 (± 0.92)	0.44 (± 2.91)
Week 69	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	0.15 (± 3.26)

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	260		
Units: Scores on a Sclae				
arithmetic mean (standard deviation)				
Week 21	0.39 (± 2.66)	0.45 (± 2.29)		
Week 69	0.43 (± 3.22)	0.61 (± 2.44)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Suicidal Ideation or Behavior, as Assessed by Columbia-Suicide Severity Rating Scale (C-SSRS) Score

End point title	Percentage of Participants With Suicidal Ideation or Behavior, as Assessed by Columbia-Suicide Severity Rating Scale (C-SSRS) Score

End point description:

SI-Suicidal Idealation, SB-Suicidal Behavior
For ODC, only Treatment Emergent Suicide-Related Events Based on the Columbia Suicide Severity Rating Scale (CSSRS) are reported.

End point type	Secondary

End point timeframe:

Screening, Baseline, Weeks 5, 13, 21, 29, 37, 45, 53, 61, 69, 77, 85, 93, 101, 117, end of treatment for early treatment termination and at early treatment termination

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	36	259
Units: Percentage				
number (not applicable)				
Suicidal Ideation (1-5) 1.Wish to Be Dead	0	8.6	2.8	9.7
SI (1-5) 2.Non-specific Active Suicidal Thoughts	0	8.6	2.8	6.9
SI(1-5) 3.ActiveSI with Methods (NoPlan)no Intent	0	2.9	0	3.5
SI(1-5) 4.Active SI Intent to Act, without Plan	0	0	0	2.3
SI(1-5) 5.Active SI with Specific Plan and Intent	0	0	0	1.9
SB(6-10) 6.PreparatoryAct or Behavior	0	0	0	0.8
Suicidal Behavior (6-10) 7) Aborted Attempt	0	0	0	0.4
Suicidal Behavior (6-10)8.Interrupted Attempt	0	0	0	0
SB(6-10) 9) Non-fatal Suicide Attempt	0	0	0	1.5
SB(6-10) 10.Completed Suicide	0	0	0	0
Self-injurious Behavior without SIntent	0	0	0	0.4
Suicidal Ideation or Behavior1-5)	0	8.6	2.8	10.0

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	260	260		
Units: Percentage				
number (not applicable)				
Suicidal Ideation (1-5) 1.Wish to Be Dead	11.2	10.4		
SI (1-5) 2.Non-specific Active Suicidal Thoughts	5.8	5.8		
SI(1-5) 3.ActiveSI with Methods (NoPlan)no Intent	3.5	4.2		
SI(1-5) 4.Active SI Intent to Act, without Plan	0.4	1.2		
SI(1-5) 5.Active SI with Specific Plan and Intent	0	1.2		
SB(6-10) 6.PreparatoryAct or Behavior	0.8	0.8		
Suicidal Behavior (6-10) 7) Aborted Attempt	0.4	0.4		
Suicidal Behavior (6-10)8.Interrupted Attempt	0.4	0.4		
SB(6-10) 9) Non-fatal Suicide Attempt	1.5	1.5		
SB(6-10) 10.Completed Suicide	0	0		
Self-injurious Behavior without SIntent	1.2	1.2		
Suicidal Ideation or Behavior1-5)	11.2	10.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of RO7234292 in Plasma

End point title	Concentration of RO7234292 in Plasma
End point description: 9999 represents values not reportable	
End point type	Secondary
End point timeframe: Baseline, Weeks 13, 21, 37, 53, 69, 85, and 101 and early treatment termination	

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	36	260
Units: ng/mL				
arithmetic mean (standard deviation)				
Week 21	0 (± 0)	0.511 (± 0.523)	0.203 (± 0.0948)	0.20 (± 0.37)
Week 69 Pre dose	9999 (± 9999)	9999 (± 9999)	0 (± 0)	1.71 (± 3.59)
Week 69 ETT	9999 (± 9999)	9999 (± 9999)	0 (± 0)	0.04 (± 0.02)

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	260[17]		
Units: ng/mL				
arithmetic mean (standard deviation)				
Week 21	0.06 (± 0.22)	0 (± 0)		
Week 69 Pre dose	0.29 (± 0.78)	0 (± 0)		
Week 69 ETT	0.03 (± 999)	0 (± 0)		

Notes:

[17] - No subjects with tominersen

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Concentration of RO7234292 in CSF

End point title	Trough Concentration of RO7234292 in CSF
End point description: 9999 represents values not reportable	
End point type	Secondary
End point timeframe: Weeks 21 and 69	

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	36	260
Units: ng/mL				
arithmetic mean (standard error)				
Week 21	0 (± 0)	4.44 (± 2.24)	1.51 (± 0.604)	1.54 (± 0.99)
Week 69	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	1.74 (± 1.08)

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	260[18]		
Units: ng/mL				
arithmetic mean (standard error)				
Week 21	0.70 (± 2.29)	0 (± 0)		
Week 69	0.55 (± 2.43)	9999 (± 9999)		

Notes:

[18] - Placebo group was not dosed with the active drug

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Anti-Drug Antibodies (ADAs).

End point title	Incidence of Anti-Drug Antibodies (ADAs).

End point description:

Data at Weeks 21 and 69 for Old Design and New Design Cohorts are reported respectively. All other timepoints were not evaluable and not meaningful. 9999 represents values not reportable

End point type	Secondary

End point timeframe:

Weeks 21 and 69

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	36	260
Units: Percentage				
number (not applicable)				
Week 21 Total Negative	9999	94.3	91.7	9999
Week 21 Negative Treatment All Samples	9999	91.4	91.7	9999
Week 21 Total Positive Treatment unaffected	9999	2.9	9999	9999
Week 69 Total Negative	9999	9999	9999	71.1
Week 69 Negative Treatment Unaffected	9999	9999	9999	0
Week 69 Total Positive	9999	9999	9999	28.9
Week 69 Positive Treatment Induced	9999	9999	9999	0

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	260		
Units: Percentage				
number (not applicable)				
Week 21 Total Negative	9999	9999		
Week 21 Negative Treatment All Samples	9999	9999		
Week 21 Total Positive Treatment unaffected	9999	9999		
Week 69 Total Negative	81.7	100		
Week 69 Negative Treatment Unaffected	1.1	0.5		

Week 69 Total Positive	18.3	22.0		
Week 69 Positive Treatment Induced	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CSF mHTT Protein Level

End point title	Change From Baseline in CSF mHTT Protein Level[19]

End point description:

To be posted in 2024. 9999 represents not applicable value.

End point type	Secondary

End point timeframe:

Baseline, Week 101

Notes:

[19] - 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 descriptive statistics was planned to be reported in the endpoint.

End point values	Placebo ODC	RO7234292 Q4W ODC	Tomi 120 mg Q8W NDC	Tomi 120mg Q16W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	36	263	264
Units: ng/mL				
arithmetic mean (standard error)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)

End point values	Placebo NDC			
Subject group type	Reporting group			
Number of subjects analysed	264			
Units: ng/mL				
arithmetic mean (standard error)	9999 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Whole and Regional Brain Volumes, as detrmined by structural magnetic resonance imaging (MRI)

End point title	Change From Baseline in Whole and Regional Brain Volumes, as detrmined by structural magnetic resonance imaging (MRI)[20]

End point description:

Analysis of Percent Change from Baseline in Volumetric MRI / BSI at 3 Months reported. Analysis performed using analysis of covariance with covariates of CAP, CAG, Age at Baseline and treatment

included. 9999 represents not evaluable data

End point type	Secondary

End point timeframe:

Week 13

Notes:

[20] - 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 descriptive statistics was planned to be reported in the endpoint.

End point values	Placebo ODC	RO7234292 Q4W ODC	Tomi 120 mg Q8W NDC	Tomi 120mg Q16W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	260	261
Units: Change in Percentage				
least squares mean (standard error)				
Change from Baseline in: Caudate Volume (mL)	0.996 (± 0.444)	0.330 (± 0.491)	9999 (± 9999)	9999 (± 9999)
Change from Baseline in: Ventricle Volume (mL)	1.537 (± 0.686)	3.785 (± 0.718)	9999 (± 9999)	9999 (± 9999)
Change from Baseline in: Whole Brain Volume (mL)	0.189 (± 0.119)	-0.184 (± 0.123)	9999 (± 9999)	9999 (± 9999)

End point values	Placebo NDC			
Subject group type	Reporting group			
Number of subjects analysed	260			
Units: Change in Percentage				
least squares mean (standard error)				
Change from Baseline in: Caudate Volume (mL)	9999 (± 9999)			
Change from Baseline in: Ventricle Volume (mL)	9999 (± 9999)			
Change from Baseline in: Whole Brain Volume (mL)	9999 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CSF Neurofilament Light Chain (NfL) Proteint Level

End point title	Change From Baseline in CSF Neurofilament Light Chain (NfL) Proteint Level

End point description:

9999 values represent not evaluable data

End point type	Secondary

End point timeframe:

Baseline, Week 101

End point values	Placebo ODC	RO7234292 Q4W ODC	RO7234292 Q8W ODC	Tomi 120 mg Q8W NDC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[21]	35[22]	36[23]	260[24]
Units: ng/mL				
geometric mean (confidence interval 95%)				
Week 21	12.233 (0.729 to 25.050)	34.548 (20.671 to 50.022)	16.553 (4.497 to 29.999)	31.893 (24.946 to 39.226)
Week 69	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)	9.996 (3.538 to 16.858)

Notes:

[21] - Data evaluable subjects included

[22] - Data evaluable subjects included

[23] - Data evaluable subjects included

[24] - Data evaluable subjects included

End point values	Tomi 120mg Q16W NDC	Placebo NDC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[25]	260[26]		
Units: ng/mL				
geometric mean (confidence interval 95%)				
Week 21	5.406 (-0.335 to 11.479)	3.365 (-2.077 to 9.109)		
Week 69	-2.559 (-8.439 to 3.699)	5.982 (-0.293 to 12.652)		

Notes:

[25] - Data evaluable subjects included

[26] - Data evaluable subjects included

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: For ODC until end of the trial, for NDC 5 moths after the last treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18

Reporting groups	
Reporting group title	PLB ODC
Reporting group description: Placebo ODC	
Reporting group title	Q4W ODC
Reporting group description: Overall Study Tomi 120mg Q4W ODC	
Reporting group title	Q8W ODC
Reporting group description: Overall Study Tomi 120mg Q8W ODC	
Reporting group title	Q8W NDC
Reporting group description: Overall Study Tomi 120mg Q8W NDC	
Reporting group title	Q16W NDC
Reporting group description: Overall Study Tomi 120mg Q16W NDC	
Reporting group title	PLB NDC
Reporting group description: Placebo ODC	

Serious adverse events	PLB ODC	Q4W ODC	Q8W ODC
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	1 / 36 (2.78%)
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)			
Rectal adenocarcinoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Vascular disorders			

Aortic aneurysm			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Subclavian artery thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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			
Asthenia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Death			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Gait disturbance			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Pyrexia			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Ill-defined disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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			
Acute respiratory failure			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Epistaxis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Choking			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Asthma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Asphyxia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Interstitial lung disease			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Pleural effusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Pulmonary embolism			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Assisted suicide			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Anxiety			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Alcoholism			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Alcohol abuse			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Delusion of parasitosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Delusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Depressed mood			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Hallucination, tactile			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Hallucination, auditory			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Depression suicidal			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Depression			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Mania			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Major depression			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Impulse-control disorder			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Mood altered			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Panic attack			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Persecutory delusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Suicide attempt			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Suicidal ideation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Bacterial test positive			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Hepatic enzyme increased			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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			
Concussion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Comminuted fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Clavicle fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Ankle fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Femoral neck fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Femur fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Fibula fracture			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Hip fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Humerus fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Pneumothorax traumatic			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Procedural headache			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (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
Post lumbar puncture syndrome			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (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
Rib fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Tibia fracture			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Stab wound			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Skin laceration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Wound haematoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Atrial fibrillation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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 / 36 (0.00%)	1 / 36 (2.78%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Chorea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Demyelination			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Depressed level of consciousness			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Dyskinesia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Dystonia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Headache			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Hydrocephalus			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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 herpetic neuralgia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Paraesthesia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Intracranial hypotension			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Presyncope			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Seizure			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Psychomotor hyperactivity			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Blood and lymphatic system disorders			
Microcytic anaemia			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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			
Intestinal perforation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Nausea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Volvulus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Ileus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Constipation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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 haemorrhage			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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			
Back pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Bursitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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 stiffness			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Periarthritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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			
Anal abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
COVID-19			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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

COVID-19 pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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 tract infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Peritonitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Meningitis aseptic			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Gastroenteritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Septic shock			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Subcutaneous abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Viral infection			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Urinary tract infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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			
Water intoxication			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Hyponatraemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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
Abnormal loss of weight			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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	Q8W NDC	Q16W NDC	PLB NDC
Total subjects affected by serious adverse events			
subjects affected / exposed	50 / 263 (19.01%)	28 / 264 (10.61%)	34 / 264 (12.88%)
number of deaths (all causes)	1	2	3
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal adenocarcinoma			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm			

subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Subclavian artery thrombosis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
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			
Asthenia			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	2 / 264 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Gait disturbance			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Pyrexia			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pain			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ill-defined disorder			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Epistaxis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Choking			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Asthma			

subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asphyxia			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Interstitial lung disease			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Pleural effusion			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Pulmonary embolism			
subjects affected / exposed	1 / 263 (0.38%)	1 / 264 (0.38%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Psychiatric disorders			
Aggression			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Assisted suicide			

subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Anxiety			
subjects affected / exposed	1 / 263 (0.38%)	1 / 264 (0.38%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcoholism			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol abuse			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Delusion of parasitosis			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delusion			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Depressed mood			

subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Hallucination, tactile			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination, auditory			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression suicidal			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Mania			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Major depression			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Impulse-control disorder			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mood altered			

subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Panic attack			
subjects affected / exposed	0 / 263 (0.00%)	2 / 264 (0.76%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Persecutory delusion			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Psychotic disorder			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	6 / 263 (2.28%)	1 / 264 (0.38%)	3 / 264 (1.14%)
occurrences causally related to treatment / all	0 / 7	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	2 / 263 (0.76%)	1 / 264 (0.38%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Bacterial test positive			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Hepatic enzyme increased			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Concussion			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Comminuted fracture			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Clavicle fracture			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	2 / 263 (0.76%)	0 / 264 (0.00%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Fall			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	2 / 264 (0.76%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			

subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Humerus fracture			
subjects affected / exposed	1 / 263 (0.38%)	1 / 264 (0.38%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	2 / 263 (0.76%)	0 / 264 (0.00%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax traumatic			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Procedural headache			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	0 / 264 (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	3 / 263 (1.14%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Tibia fracture			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	2 / 264 (0.76%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			

subjects affected / exposed	4 / 263 (1.52%)	0 / 264 (0.00%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stab wound			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Skin laceration			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Wound haematoma			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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			
Ataxia			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Chorea			

subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Demyelination			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Depressed level of consciousness			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Dyskinesia			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Dystonia			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	2 / 263 (0.76%)	0 / 264 (0.00%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post herpetic neuralgia			

subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Paraesthesia			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial hypotension			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Presyncope			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Transient ischaemic attack			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Seizure			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Microcytic anaemia			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Ear and labyrinth disorders			

Vertigo positional			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Gastrointestinal disorders			
Intestinal perforation			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Nausea			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volvulus			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Ileus			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Constipation			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Bursitis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Intervertebral disc protrusion			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Musculoskeletal stiffness			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periarthritis			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
COVID-19			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
COVID-19 pneumonia			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory tract infection			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Pneumonia			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Peritonitis			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Subcutaneous abscess			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Viral infection			
subjects affected / exposed	0 / 263 (0.00%)	1 / 264 (0.38%)	0 / 264 (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
Urinary tract infection			

subjects affected / exposed	0 / 263 (0.00%)	2 / 264 (0.76%)	0 / 264 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Water intoxication			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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
Abnormal loss of weight			
subjects affected / exposed	1 / 263 (0.38%)	0 / 264 (0.00%)	0 / 264 (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

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

Non-serious adverse events	PLB ODC	Q4W ODC	Q8W ODC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 36 (66.67%)	23 / 36 (63.89%)	19 / 36 (52.78%)
Investigations			
CSF protein increased			
subjects affected / exposed	0 / 36 (0.00%)	3 / 36 (8.33%)	0 / 36 (0.00%)
occurrences (all)	0	3	0
Injury, poisoning and procedural complications			
Inappropriate schedule of product administration			
subjects affected / exposed	3 / 36 (8.33%)	1 / 36 (2.78%)	0 / 36 (0.00%)
occurrences (all)	3	1	0
Fall			
subjects affected / exposed	4 / 36 (11.11%)	2 / 36 (5.56%)	4 / 36 (11.11%)
occurrences (all)	6	2	6
Contusion			

subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	2 / 36 (5.56%)
occurrences (all)	1	0	2
Post lumbar puncture syndrome			
subjects affected / exposed	4 / 36 (11.11%)	3 / 36 (8.33%)	7 / 36 (19.44%)
occurrences (all)	6	6	8
Procedural pain			
subjects affected / exposed	4 / 36 (11.11%)	6 / 36 (16.67%)	5 / 36 (13.89%)
occurrences (all)	8	11	9
Skin laceration			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	3	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Nervous system disorders			
Somnolence			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	2 / 36 (5.56%)
occurrences (all)	1	0	2
Paraesthesia			
subjects affected / exposed	3 / 36 (8.33%)	2 / 36 (5.56%)	2 / 36 (5.56%)
occurrences (all)	4	2	4
Headache			
subjects affected / exposed	6 / 36 (16.67%)	3 / 36 (8.33%)	4 / 36 (11.11%)
occurrences (all)	9	3	6
Dizziness			
subjects affected / exposed	3 / 36 (8.33%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences (all)	4	0	1
Tremor			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	0 / 36 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	0 / 36 (0.00%)
occurrences (all)	0	2	0
Puncture site pain			

subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	2 / 36 (5.56%)
occurrences (all)	0	3	2
Pyrexia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	1 / 36 (2.78%)
occurrences (all)	0	1	2
Gait disturbance			
subjects affected / exposed	0 / 36 (0.00%)	4 / 36 (11.11%)	1 / 36 (2.78%)
occurrences (all)	0	4	2
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	2 / 36 (5.56%)
occurrences (all)	1	1	2
Nausea			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	2 / 36 (5.56%)
occurrences (all)	2	3	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	1 / 36 (2.78%)
occurrences (all)	0	2	1
Anxiety			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	4 / 36 (11.11%)	1 / 36 (2.78%)	4 / 36 (11.11%)
occurrences (all)	4	2	4
Pain in extremity			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	2 / 36 (5.56%)
occurrences (all)	1	2	2
Infections and infestations			

Urinary tract infection			
subjects affected / exposed	2 / 36 (5.56%)	4 / 36 (11.11%)	2 / 36 (5.56%)
occurrences (all)	2	5	2
Fungal infection			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	0 / 36 (0.00%)
occurrences (all)	0	2	0
Nasopharyngitis			
subjects affected / exposed	3 / 36 (8.33%)	1 / 36 (2.78%)	1 / 36 (2.78%)
occurrences (all)	3	1	1

Non-serious adverse events	Q8W NDC	Q16W NDC	PLB NDC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	204 / 263 (77.57%)	187 / 264 (70.83%)	193 / 264 (73.11%)
Investigations			
CSF protein increased			
subjects affected / exposed	13 / 263 (4.94%)	1 / 264 (0.38%)	2 / 264 (0.76%)
occurrences (all)	13	1	2
Injury, poisoning and procedural complications			
Inappropriate schedule of product administration			
subjects affected / exposed	1 / 263 (0.38%)	2 / 264 (0.76%)	1 / 264 (0.38%)
occurrences (all)	2	3	2
Fall			
subjects affected / exposed	70 / 263 (26.62%)	63 / 264 (23.86%)	79 / 264 (29.92%)
occurrences (all)	136	141	170
Contusion			
subjects affected / exposed	16 / 263 (6.08%)	15 / 264 (5.68%)	18 / 264 (6.82%)
occurrences (all)	19	20	30
Post lumbar puncture syndrome			
subjects affected / exposed	24 / 263 (9.13%)	18 / 264 (6.82%)	21 / 264 (7.95%)
occurrences (all)	34	28	39
Procedural pain			
subjects affected / exposed	23 / 263 (8.75%)	21 / 264 (7.95%)	22 / 264 (8.33%)
occurrences (all)	51	31	29
Skin laceration			
subjects affected / exposed	12 / 263 (4.56%)	5 / 264 (1.89%)	8 / 264 (3.03%)
occurrences (all)	14	5	11

Vascular disorders			
Haematoma			
subjects affected / exposed	3 / 263 (1.14%)	3 / 264 (1.14%)	3 / 264 (1.14%)
occurrences (all)	3	5	5
Nervous system disorders			
Somnolence			
subjects affected / exposed	10 / 263 (3.80%)	4 / 264 (1.52%)	5 / 264 (1.89%)
occurrences (all)	15	4	5
Paraesthesia			
subjects affected / exposed	7 / 263 (2.66%)	8 / 264 (3.03%)	6 / 264 (2.27%)
occurrences (all)	10	10	10
Headache			
subjects affected / exposed	61 / 263 (23.19%)	57 / 264 (21.59%)	59 / 264 (22.35%)
occurrences (all)	150	105	114
Dizziness			
subjects affected / exposed	20 / 263 (7.60%)	22 / 264 (8.33%)	17 / 264 (6.44%)
occurrences (all)	33	31	19
Tremor			
subjects affected / exposed	2 / 263 (0.76%)	0 / 264 (0.00%)	0 / 264 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	10 / 263 (3.80%)	17 / 264 (6.44%)	10 / 264 (3.79%)
occurrences (all)	13	20	10
Puncture site pain			
subjects affected / exposed	24 / 263 (9.13%)	13 / 264 (4.92%)	24 / 264 (9.09%)
occurrences (all)	45	17	46
Pyrexia			
subjects affected / exposed	12 / 263 (4.56%)	14 / 264 (5.30%)	13 / 264 (4.92%)
occurrences (all)	13	17	16
Gait disturbance			
subjects affected / exposed	10 / 263 (3.80%)	3 / 264 (1.14%)	2 / 264 (0.76%)
occurrences (all)	11	3	2
Gastrointestinal disorders			
Vomiting			

subjects affected / exposed	14 / 263 (5.32%)	16 / 264 (6.06%)	16 / 264 (6.06%)
occurrences (all)	17	22	20
Nausea			
subjects affected / exposed	12 / 263 (4.56%)	12 / 264 (4.55%)	15 / 264 (5.68%)
occurrences (all)	14	17	19
Diarrhoea			
subjects affected / exposed	17 / 263 (6.46%)	15 / 264 (5.68%)	19 / 264 (7.20%)
occurrences (all)	20	16	20
Psychiatric disorders			
Insomnia			
subjects affected / exposed	11 / 263 (4.18%)	15 / 264 (5.68%)	13 / 264 (4.92%)
occurrences (all)	14	16	16
Anxiety			
subjects affected / exposed	16 / 263 (6.08%)	11 / 264 (4.17%)	15 / 264 (5.68%)
occurrences (all)	20	12	16
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	19 / 263 (7.22%)	12 / 264 (4.55%)	22 / 264 (8.33%)
occurrences (all)	22	13	32
Back pain			
subjects affected / exposed	57 / 263 (21.67%)	58 / 264 (21.97%)	49 / 264 (18.56%)
occurrences (all)	91	93	92
Pain in extremity			
subjects affected / exposed	19 / 263 (7.22%)	14 / 264 (5.30%)	15 / 264 (5.68%)
occurrences (all)	30	16	20
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	13 / 263 (4.94%)	13 / 264 (4.92%)	8 / 264 (3.03%)
occurrences (all)	20	14	18
Fungal infection			
subjects affected / exposed	0 / 263 (0.00%)	0 / 264 (0.00%)	1 / 264 (0.38%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	36 / 263 (13.69%)	28 / 264 (10.61%)	44 / 264 (16.67%)
occurrences (all)	48	40	61

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported