Clinical trial results:
An Open-Label Extension Study to Evaluate the Long-Term Safety and Tolerability of Intrathecally Administered RO7234292 (RG6042) in Patients with Huntington's Disease

Summary

EudraCT number	2018-003898-94
Trial protocol	GB ES NL AT IT
Global end of trial date	23 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	BN40955

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03842969
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, Hoffmann-La Roche, +41 61 6878333, genentech@druginfo.com
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	27 January 2023
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	23 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will evaluate the long-term safety and tolerability of RO7234292 (RG6042) in participants who have completed other F. Hoffmann-La Roche, Ltd.-sponsored and/or Genentech-sponsored studies in the Huntington's disease (HD) in the development program for RG6042.

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 April 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	Austria: 1
Country: Number of subjects enrolled	Canada: 24
Country: Number of subjects enrolled	Germany: 55
Country: Number of subjects enrolled	Spain: 47
Country: Number of subjects enrolled	United Kingdom: 42
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	United States: 79
Worldwide total number of subjects	251
EEA total number of subjects	106

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)	238
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study consists Period 1 and 2. All participants (17) in the Q4W arm stopped Q4W dosing (Period 1) and 15 participants continued into Period 2.

Pre-assignment

Screening details:

15 participants from Period 1 Q4W were re-randomized to receive Tominersen 120 mg Q8W or Q16W in Period 2.

Period 1

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

Blinding implementation details:

For "Mutually Exclusive Arm" Description: The study has non-mutually exclusive arms. 15 patients are transferred between arms

Arms

Are arms mutually exclusive?	Yes
Arm title	Period 1 Tominersen 120mg Q4W

Arm description:

Participants received open-label RO7234292 Q4W in this Period 1

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

Dosage and administration details:

Open-label RO7234292 Q4W

Arm title	Period 2 Tominersen 120mg Q8W

Arm description:

Participants received open-label RO7234292 Q8W in this Period 2

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

Dosage and administration details:

Open-label RO7234292 Q8W

Arm title	Period 2 Tominersen 120mg Q16W

Arm description:

Participants received open-label RO7234292 Q16W in this Period 2

Arm type	Experimental

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

Dosage and administration details:

Open-label RO7234292 Q16W

Number of subjects in period 1	Period 1 Tominersen 120mg Q4W	Period 2 Tominersen 120mg Q8W	Period 2 Tominersen 120mg Q16W
Started	17	146	88
Completed	0	0	0
Not completed	17	146	88
Adverse event, serious fatal	1	-	1
Consent withdrawn by subject	3	30	20
Physician decision	-	3	-
Adverse event, non-fatal	-	2	-
Pregnancy	-	-	1
Participant declined follow-up visit	-	1	-
Lost to follow-up	-	2	-
terminated by sponsor	12	106	66
Protocol deviation	1	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Period 1 Tominersen 120mg Q4W
Reporting group description:	
Participants received open-label RO7234292 Q4W in this Period 1	
Reporting group title	Period 2 Tominersen 120mg Q8W
Reporting group description:	
Participants received open-label RO7234292 Q8W in this Period 2	
Reporting group title	Period 2 Tominersen 120mg Q16W
Reporting group description:	
Participants received open-label RO7234292 Q16W in this Period 2	

Reporting group values	Period 1 Tominersen 120mg Q4W	Period 2 Tominersen 120mg Q8W	Period 2 Tominersen 120mg Q16W
Number of subjects	17	146	88
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)	16	141	81
From 65-84 years	1	5	7
85 years and over	0	0	0
Age Continuous Units: Number			
arithmetic mean	50.4	47.9	48.6
standard deviation	± 8.9	± 9.7	± 10.9
Sex: Female, Male Units:			
Female	6	73	40
Male	11	73	48
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	2	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	2	0
White	17	140	83
More than one race	0	1	1
Unknown or Not Reported	0	1	3
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	13	7

Not Hispanic or Latino	17	133	81
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	251		
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)	238		
From 65-84 years	13		
85 years and over	0		
Age Continuous Units: Number			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units:			
Female	119		
Male	132		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	3		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	2		
White	240		
More than one race	2		
Unknown or Not Reported	4		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	20		
Not Hispanic or Latino	231		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Period 1 Tominersen 120mg Q4W
Reporting group description: Participants received open-label RO7234292 Q4W in this Period 1	
Reporting group title	Period 2 Tominersen 120mg Q8W
Reporting group description: Participants received open-label RO7234292 Q8W in this Period 2	
Reporting group title	Period 2 Tominersen 120mg Q16W
Reporting group description: Participants received open-label RO7234292 Q16W in this Period 2	
Subject analysis set title	Tomi 120mg Q4W (Period 1)
Subject analysis set type	Safety analysis
Subject analysis set description: Period 1 Tominersen 120mg Q4W Participants received open-label RO7234292 Q4W in this Period 1	
Subject analysis set title	Tomi 120mg Q8W (Prior Q4w)
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received open-label RO7234292 Q8W after having received Q4W treatment previously	
Subject analysis set title	Period 2 Tominersen 120mg Q8W (No Loading)
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received open-label RO7234292 Q8W without prior treatment with RO7234292	
Subject analysis set title	Period 2 Tominersen 120mg Q8W (With Loading)
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received open-label RO7234292 Q8W with prior treatment with RO7234292 Q8W	
Subject analysis set title	Period 2 Tominersen 120mg Q8W (Prior BP40410)
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received open-label RO7234292 Q8W with prior treatment with RO7234292 Q4W in study BP40410	
Subject analysis set title	Period 2 Tominersen 120mg Q16W (Prior Q4W)
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received open-label RO7234292 Q16W after having received Q4W treatment previously	
Subject analysis set title	Period 2 Tominersen 120mg Q16W (No Loading)
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received open-label RO7234292 Q16W without prior treatment with RO7234292	
Subject analysis set title	Period 2 Tominersen 120mg Q16W (Prior BP40410)
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received open-label RO7234292 Q16W with prior treatment with RO7234292 Q4W in study BP40410	

Primary: Percentage of Participants with Adverse Events

End point title	Percentage of Participants with Adverse Events[1]

End point description:

The reported are the treatment-emergent AEs with an onset date up to 5 months after last study drug intake.

End point type	Primary

End point timeframe:

Up to Approximately 3 Years

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	Period 1 Tominersen 120mg Q4W	Period 2 Tominersen 120mg Q8W	Period 2 Tominersen 120mg Q16W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	143	88	
Units: Percentage of Participants				
number (not applicable)	71.4	83.9	81.8	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Suicidal Ideation, Suicidal Behavior, and Self-Injurious Behavior without Suicidal Intent Based on the Columbia Suicide Severity Rating Scale (C-SSRS)

End point title	Number of Participants with Suicidal Ideation, Suicidal Behavior, and Self-Injurious Behavior without Suicidal Intent Based on the Columbia Suicide Severity Rating Scale (C-SSRS)[2]

End point description:

C-SSRS assesses Suicidal Ideation behavior. 4 constructs measured: severity of ideation, intensity of ideation, behavior, and lethality of actual suicide attempts. Yes/No data collected for 10 categories, composite endpoints based on the categories are followed over time to monitor safety. Composite endpoint of suicidal ideation (1-5), n and (%) number and % of who experience any of 5 suicidal ideation events at least 1 after receiving 1st dose of study medication. Composite endpoint of suicidal behavior (6-10), n and (%) are the number and % of patients experienced any 1of 5 suicidal behavior events at least 1 after receiving the 5 dose of study medication. Composite endpoint of suicidal ideation or behavior (1-10), n and (%) are the number and % of patients experienced any 1 the 10 SI or behavior events at least 1 after receiving 1st dose of study medication.
SI-Suicidal Idealization; AS-Active Suicidal; ASI-Active Suicidal Intention; IoA-Intent of Act

End point type	Primary

End point timeframe:

Up to approximately 3 Years

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	Period 1 Tominersen 120mg Q4W	Period 2 Tominersen 120mg Q8W	Period 2 Tominersen 120mg Q16W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	143	88	
Units: Number of participants				
Suicidal Ideation (1-5) -Wish to Be Dead	1	16	3	
Suicidal Ideation (1-5) -Non-specific AS Thoughts	0	9	1	
SI(1-5)ASI with Methods-NoPlan without IoA	0	7	1	
SI(1-5) ASI with IoA, without Specific Plan	0	3	1	
SI (1-5)-AS Ideation with Specific Plan and Intent	0	2	0	
SI Behavior (6-10)-Preparatory Acts or Behavior	0	1	0	
Suicidal Behavior (6-10) -Aborted Attempt	0	0	0	
Suicidal Behavior (6-10) -Interrupted Attempt	0	1	0	
Suicidal Behavior(6-10) Non-fatal Suicide Attempt	0	2	0	
Suicidal Behavior(6-10) -Completed Suicide	0	0	0	
Suicidal Ideation or Behavior(1-10)	1	16	3	
Self-injurious Behavior without Suicidal Intent	0	1	0	
Treatment-Emergent Suicidal Ideation	0	14	2	
Treatment-Emergent Serious Suicidal Ideation	0	3	1	
Emergence of Serious Suicidal Ideation	0	2	1	
Emergence of Suicidal Behavior	0	3	0	

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Cognition, using Montreal Cognitive Assessment (MoCA)

End point title	Change From Baseline in Cognition, using Montreal Cognitive Assessment (MoCA)[3]

End point description:

MoCA contains a series of basic assessments, including attention and visuospatial tasks. The total score ranges from 0−30, where lower scores indicate greater impairment.
SD values marked 999 entails Not Estimable values. MOCA01-Total scores are reported which includes the sub-categories reported below.
The data presented are absolute scores for baseline and change from baseline for post-baseline assessments.

The value 999 represent no subjects per analysis or not evaluable values.

End point type	Primary

End point timeframe:

Up to Approximately 3 Years

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Tomi 120mg Q4W (Period 1)	Tomi 120mg Q8W (Prior Q4w)	Period 2 Tominersen 120mg Q8W (No Loading)	Period 2 Tominersen 120mg Q8W (With Loading)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	25	72	43
Units: Scores of a Scale				
arithmetic mean (standard deviation)				
MOCA01-Total Baseline	24.50 (± 3.98)	25.08 (± 3.49)	24.92 (± 3.47)	24.62 (± 4.44)
MOCA01-Total Week 17	-4.00 (± 999)	0.46 (± 2.19)	0.16 (± 2.58)	0.19 (± 2.56)
MOCA01-Total Week 25	3.00 (± 999)	999 (± 999)	999 (± 999)	999 (± 999)
MOCA01-Total Week 33	3.00 (± 999)	0.16 (± 1.74)	0.28 (± 2.61)	0.35 (± 1.76)
MOCA01-Total Week 49	999 (± 999)	0.33 (± 2.33)	-0.39 (± 2.83)	-0.08 (± 2.26)
MOCA01-Total Week 65	999 (± 999)	-0.09 (± 2.09)	-0.08 (± 2.56)	-0.08 (± 1.91)
MOCA01-Total Week 81	999 (± 999)	0.59 (± 1.30)	-0.38 (± 3.31)	-0.09 (± 1.95)
MOCA01-Total Week 97	999 (± 999)	-0.47 (± 2.06)	-0.97 (± 3.12)	0.45 (± 2.20)
MOCA01-Total Week 113	999 (± 999)	0.18 (± 1.94)	-0.36 (± 2.65)	0.10 (± 2.62)
MOCA01-Total Week 129	999 (± 999)	-0.75 (± 1.22)	-0.50 (± 1.95)	-0.15 (± 3.48)
MOCA01-Total Week 145	999 (± 999)	0.33 (± 1.53)	999 (± 999)	-4.83 (± 5.91)

End point values	Period 2 Tominersen 120mg Q8W (Prior BP40410)	Period 2 Tominersen 120mg Q16W (Prior Q4W)	Period 2 Tominersen 120mg Q16W (No Loading)	Period 2 Tominersen 120mg Q16W (Prior BP40410)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	24	60	4
Units: Scores of a Scale				
arithmetic mean (standard deviation)				
MOCA01-Total Baseline	25.33 (± 1.53)	23.43 (± 4.49)	24.03 (± 3.88)	19.75 (± 4.35)
MOCA01-Total Week 17	-1.00 (± 1.00)	-0.57 (± 2.01)	-0.17 (± 2.79)	3.25 (± 2.36)
MOCA01-Total Week 25	999 (± 999)	999 (± 999)	999 (± 999)	999 (± 999)
MOCA01-Total Week 33	0.67 (± 2.08)	-0.90 (± 2.76)	0.32 (± 2.44)	2.25 (± 2.22)
MOCA01-Total Week 49	-0.67 (± 3.06)	-0.40 (± 2.68)	-0.13 (± 2.53)	3.00 (± 3.46)
MOCA01-Total Week 65	-5.00 (± 999)	-0.43 (± 2.86)	0.27 (± 2.85)	0.50 (± 3.54)
MOCA01-Total Week 81	-2.00 (± 999)	0.25 (± 2.57)	-0.24 (± 2.90)	0.50 (± 3.54)
MOCA01-Total Week 97	999 (± 999)	0.24 (± 2.46)	-0.46 (± 3.01)	999 (± 999)
MOCA01-Total Week 113	999 (± 999)	0.19 (± 2.51)	0.36 (± 3.01)	999 (± 999)
MOCA01-Total Week 129	999 (± 999)	-0.11 (± 1.90)	2.20 (± 3.19)	999 (± 999)
MOCA01-Total Week 145	999 (± 999)	0.00 (± 999)	999 (± 999)	999 (± 999)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to Approx. 3 Years	
Adverse event reporting additional description:	
Treatment-emergent with onset before 5 months after last dose	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18

Reporting groups	
Reporting group title	Period 1 Tominersen 120mg Q4W
Reporting group description:	
Period 1 Tominersen 120mg Q4W	
Reporting group title	Period 2 Tominersen 120mg Q16W
Reporting group description:	
Period 2 Tominersen 120mg Q16W	
Reporting group title	Period 2 Tominersen 120mg Q8W
Reporting group description:	
Period 2 Tominersen 120mg Q8W	

Serious adverse events	Period 1 Tominersen 120mg Q4W	Period 2 Tominersen 120mg Q16W	Period 2 Tominersen 120mg Q8W
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 14 (7.14%)	9 / 88 (10.23%)	17 / 143 (11.89%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 14 (0.00%)	1 / 88 (1.14%)	0 / 143 (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
Surgical and medical procedures			
Euthanasia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 88 (0.00%)	0 / 143 (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
General disorders and administration site conditions			
Gait disturbance			

subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cyst			
subjects affected / exposed	0 / 14 (0.00%)	1 / 88 (1.14%)	0 / 143 (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			
Acute stress disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
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	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dissociative disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 88 (1.14%)	0 / 143 (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
Suicidal behaviour			
subjects affected / exposed	0 / 14 (0.00%)	1 / 88 (1.14%)	0 / 143 (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 / 14 (0.00%)	2 / 88 (2.27%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritability			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
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			
Fall			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral injury			
subjects affected / exposed	0 / 14 (0.00%)	1 / 88 (1.14%)	0 / 143 (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
Concussion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Phimosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Arachnoiditis			

subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinsonism			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Normal pressure hydrocephalus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chorea			
subjects affected / exposed	0 / 14 (0.00%)	1 / 88 (1.14%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Balance disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ataxia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 88 (1.14%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
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			
Blood loss anaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 88 (1.14%)	0 / 143 (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
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 14 (0.00%)	1 / 88 (1.14%)	0 / 143 (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
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 14 (0.00%)	1 / 88 (1.14%)	0 / 143 (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
Meningitis aseptic			
subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 88 (1.14%)	0 / 143 (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
Metabolism and nutrition disorders			
Hypokalaemia			

subjects affected / exposed	0 / 14 (0.00%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Period 1 Tominersen 120mg Q4W	Period 2 Tominersen 120mg Q16W	Period 2 Tominersen 120mg Q8W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 14 (85.71%)	56 / 88 (63.64%)	99 / 143 (69.23%)
Vascular disorders			
Haematoma			
subjects affected / exposed	2 / 14 (14.29%)	3 / 88 (3.41%)	1 / 143 (0.70%)
occurrences (all)	2	4	1
Lymphoedema			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 14 (7.14%)	4 / 88 (4.55%)	5 / 143 (3.50%)
occurrences (all)	1	5	5
Gait disturbance			
subjects affected / exposed	0 / 14 (0.00%)	5 / 88 (5.68%)	3 / 143 (2.10%)
occurrences (all)	0	5	4
Oedema peripheral			
subjects affected / exposed	1 / 14 (7.14%)	0 / 88 (0.00%)	2 / 143 (1.40%)
occurrences (all)	1	0	3
Respiratory, thoracic and mediastinal disorders			
Sinus congestion			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	1	0
Rhinitis allergic			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			

Insomnia			
subjects affected / exposed	1 / 14 (7.14%)	6 / 88 (6.82%)	17 / 143 (11.89%)
occurrences (all)	1	6	17
Depression			
subjects affected / exposed	1 / 14 (7.14%)	4 / 88 (4.55%)	6 / 143 (4.20%)
occurrences (all)	1	5	6
Depressed mood			
subjects affected / exposed	1 / 14 (7.14%)	2 / 88 (2.27%)	2 / 143 (1.40%)
occurrences (all)	1	3	2
Anxiety			
subjects affected / exposed	2 / 14 (14.29%)	7 / 88 (7.95%)	6 / 143 (4.20%)
occurrences (all)	2	8	6
Affect lability			
subjects affected / exposed	1 / 14 (7.14%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences (all)	1	0	2
Irritability			
subjects affected / exposed	2 / 14 (14.29%)	6 / 88 (6.82%)	4 / 143 (2.80%)
occurrences (all)	3	8	4
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences (all)	1	0	2
CSF protein increased			
subjects affected / exposed	1 / 14 (7.14%)	4 / 88 (4.55%)	2 / 143 (1.40%)
occurrences (all)	1	5	3
Vitamin D decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences (all)	1	0	2
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	1	0
Contusion			
subjects affected / exposed	2 / 14 (14.29%)	6 / 88 (6.82%)	16 / 143 (11.19%)
occurrences (all)	2	9	28
Eye contusion			

subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	1	0
Fall			
subjects affected / exposed	7 / 14 (50.00%)	21 / 88 (23.86%)	44 / 143 (30.77%)
occurrences (all)	50	145	110
Foreign body aspiration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences (all)	1	0	2
Periorbital haematoma			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	1	0
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 14 (0.00%)	2 / 88 (2.27%)	11 / 143 (7.69%)
occurrences (all)	0	2	12
Procedural pain			
subjects affected / exposed	2 / 14 (14.29%)	6 / 88 (6.82%)	19 / 143 (13.29%)
occurrences (all)	2	7	33
Skin abrasion			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	7 / 143 (4.90%)
occurrences (all)	10	15	15
Skin laceration			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	9 / 143 (6.29%)
occurrences (all)	1	1	13
Spinal compression fracture			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	1 / 143 (0.70%)
occurrences (all)	1	1	1
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	1 / 143 (0.70%)
occurrences (all)	1	1	3
Aphasia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences (all)	1	0	1
Ataxia			
subjects affected / exposed	1 / 14 (7.14%)	2 / 88 (2.27%)	3 / 143 (2.10%)
occurrences (all)	1	2	3

Balance disorder			
subjects affected / exposed	1 / 14 (7.14%)	4 / 88 (4.55%)	1 / 143 (0.70%)
occurrences (all)	1	4	1
Cerebellar atrophy			
subjects affected / exposed	1 / 14 (7.14%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences (all)	1	0	2
Cerebral ventricle dilatation			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	4 / 143 (2.80%)
occurrences (all)	1	2	4
Coordination abnormal			
subjects affected / exposed	1 / 14 (7.14%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences (all)	1	0	1
Dizziness			
subjects affected / exposed	0 / 14 (0.00%)	1 / 88 (1.14%)	8 / 143 (5.59%)
occurrences (all)	0	1	9
Dysarthria			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	1 / 143 (0.70%)
occurrences (all)	2	1	2
Extensor plantar response			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	2	0
Headache			
subjects affected / exposed	0 / 14 (0.00%)	6 / 88 (6.82%)	13 / 143 (9.09%)
occurrences (all)	0	6	25
Hypotonia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 88 (0.00%)	1 / 143 (0.70%)
occurrences (all)	1	0	2
Memory impairment			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	3 / 143 (2.10%)
occurrences (all)	1	1	3
Motor dysfunction			
subjects affected / exposed	1 / 14 (7.14%)	0 / 88 (0.00%)	2 / 143 (1.40%)
occurrences (all)	2	0	3
Parkinsonism			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	2	3	0

Pleocytosis			
subjects affected / exposed	1 / 14 (7.14%)	2 / 88 (2.27%)	8 / 143 (5.59%)
occurrences (all)	2	2	16
Post-traumatic headache			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	1	0
Restless legs syndrome			
subjects affected / exposed	1 / 14 (7.14%)	0 / 88 (0.00%)	2 / 143 (1.40%)
occurrences (all)	1	0	2
Syncope			
subjects affected / exposed	0 / 14 (0.00%)	6 / 88 (6.82%)	1 / 143 (0.70%)
occurrences (all)	0	7	1
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	2 / 143 (1.40%)
occurrences (all)	1	1	2
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 14 (7.14%)	5 / 88 (5.68%)	9 / 143 (6.29%)
occurrences (all)	1	6	9
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	2 / 143 (1.40%)
occurrences (all)	1	1	2
Skin and subcutaneous tissue disorders			
Pigmentation disorder			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 14 (0.00%)	3 / 88 (3.41%)	8 / 143 (5.59%)
occurrences (all)	0	3	9
Back pain			

subjects affected / exposed	2 / 14 (14.29%)	14 / 88 (15.91%)	19 / 143 (13.29%)
occurrences (all)	2	15	24
Bursitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 88 (0.00%)	3 / 143 (2.10%)
occurrences (all)	1	0	3
Enthesopathy			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	2	0
Exostosis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	2	0
Fracture pain			
subjects affected / exposed	1 / 14 (7.14%)	2 / 88 (2.27%)	0 / 143 (0.00%)
occurrences (all)	1	2	0
Limb mass			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	1 / 143 (0.70%)
occurrences (all)	1	2	1
Psoriatic arthropathy			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	2	0
Spinal osteoarthritis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	2	0
Vertebral foraminal stenosis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	2	0
Vertebral osteophyte			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	2	0
Infections and infestations			
Injection site infection			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	0 / 143 (0.00%)
occurrences (all)	1	1	0

Nasopharyngitis			
subjects affected / exposed	0 / 14 (0.00%)	3 / 88 (3.41%)	13 / 143 (9.09%)
occurrences (all)	0	3	15
Onychomycosis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	1 / 143 (0.70%)
occurrences (all)	1	2	1
Tooth infection			
subjects affected / exposed	1 / 14 (7.14%)	1 / 88 (1.14%)	2 / 143 (1.40%)
occurrences (all)	1	1	3
Urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)	4 / 88 (4.55%)	5 / 143 (3.50%)
occurrences (all)	1	5	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 April 2021	Protocol v 7

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported