Clinical trial results:
A Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of RO7234292 (ISIS 443139) in Huntington's Disease Subjects who Participated in Prior Investigational Studies of RO7234292 (ISIS 443139)

Summary

EudraCT number	2017-002471-25
Trial protocol	GB DE
Global end of trial date	08 October 2019

Results information

Result version number	v2 (current)
This version publication date	17 February 2022
First version publication date	13 November 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	BN40697

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03342053
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	Medical Communications, Hoffmann-La Roche, +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study tested the safety, tolerability, pharmacokinetics and pharmacodynamics of RO7234292 administered intrathecally to adult patients with Huntington's Disease.

Protection of trial subjects:

This study was conducted in accordance with the protocol and with the following: ● Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines ● Applicable ICH Good Clinical Practice (GCP) Guidelines ● Applicable laws and regulations

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 January 2018
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	Canada: 6
Country: Number of subjects enrolled	Germany: 19
Country: Number of subjects enrolled	United Kingdom: 21
Worldwide total number of subjects	46
EEA total number of subjects	19

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)	43
From 65 to 84 years	3

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participant eligibility for the study was determined within 4 weeks prior to participant entry into the Treatment Period.

Pre-assignment

Screening details:

This study is an OLE for patients who participated in Study ISIS 443139-CS1. Each subject was assigned to the same screening and subject identification numbers as in the prior MAD study (Study ISIS 443139-CS1).

Period 1

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

Blinding implementation details:

Randomised, open label with no control

Arms

Are arms mutually exclusive?	Yes
Arm title	RO7234292 Monthly

Arm description:

RO7234292 was administered intrathecally every 28 days for 14 months.

Arm type	Experimental
Investigational medicinal product name	RO7234292 (RG6042)
Investigational medicinal product code	
Other name	Tominersen
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

RO7234292 is administered intrathecally every 28 days for 14 months at a dose of 120mg.

Arm title	RO7234292 Bimonthly

Arm description:

RO7234292 was administered intrathecally every 56 days for 14 months following 2 monthly doses to serve as a loading dose.

Arm type	Experimental
Investigational medicinal product name	RO7234292 (RG6042)
Investigational medicinal product code	
Other name	Tominersen
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

RO7234292 is administered intrathecally every 56 days at a dose of 120mg for 14 months following 2 monthly doses to serve as a loading dose.

Number of subjects in period 1	RO7234292 Monthly	RO7234292 Bimonthly
Started	23	23
Completed	21	22
Not completed	2	1
Adverse event, serious fatal	1	-
Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups	
Reporting group title	RO7234292 Monthly
Reporting group description:	
RO7234292 was administered intrathecally every 28 days for 14 months.	
Reporting group title	RO7234292 Bimonthly
Reporting group description:	
RO7234292 was administered intrathecally every 56 days for 14 months following 2 monthly doses to serve as a loading dose.	

Reporting group values	RO7234292 Monthly	RO7234292 Bimonthly	Total
Number of subjects	23	23	46
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	23	20	43
>=65 years	0	3	3
Age Continuous Units: Years			
arithmetic mean	47.7	49.5	
standard deviation	± 9.3	± 11.3	-
Sex: Female, Male Units: Participants			
Female	8	10	18
Male	15	13	28
Race (NIH/OMB)			
One participant's race is known, was reported but cannot be classified in Roche database.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	22	23	45
More than one race	0	0	0
Other	1	0	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	23	23	46
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	RO7234292 Monthly
Reporting group description:	
RO7234292 was administered intrathecally every 28 days for 14 months.	
Reporting group title	RO7234292 Bimonthly
Reporting group description:	
RO7234292 was administered intrathecally every 56 days for 14 months following 2 monthly doses to serve as a loading dose.	

Primary: Percentage of Participants with Treatment-Emergent Adverse Events (AEs)

End point title	Percentage of Participants with Treatment-Emergent Adverse Events (AEs)[1]
End point description:	
Descriptive summary of percentage of participants with treatment emergent AEs	
End point type	Primary
End point timeframe:	
From baseline up to 1 year 9 months	

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	RO7234292 Monthly	RO7234292 Bimonthly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: Percentage				
number (not applicable)				
Percentage of Subjects with Treatment-Emergent AEs	100	95.7		

Statistical analyses

No statistical analyses for this end point

Secondary: RO7234292 CSF Trough Concentrations by Study Day Prior to Monthly and Bimonthly IT Administration of 120 mg RO7234292 (Primary Analysis)

End point title	RO7234292 CSF Trough Concentrations by Study Day Prior to Monthly and Bimonthly IT Administration of 120 mg RO7234292 (Primary Analysis)
End point description:	
Here "9999" means that value is not available (NA). Data for Bi-monthly arm was not collected on days 57, 113, 169, 225, 281, 337, 393.	
End point type	Secondary
End point timeframe:	
From baseline to Day 421	

End point values	RO7234292 Monthly	RO7234292 Bimonthly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: ng/mL				
geometric mean (full range (min-max))				
Day 29	2.59 (1.31 to 12.7)	2.52 (0.817 to 7.85)		
Day 57	3.47 (1.43 to 19.2)	9999 (9999 to 9999)		
Day 85	3.70 (1.38 to 7.34)	1.39 (0.164 to 5.74)		
Day 113	3.97 (1.96 to 16.4)	9999 (9999 to 9999)		
Day 141	4.57 (1.72 to 13)	1.35 (0.396 to 3.69)		
Day 169	4.47 (2.04 to 12.7)	9999 (9999 to 9999)		
Day 197	4.58 (1.74 to 8.61)	1.26 (0.281 to 3.37)		
Day 225	5.21 (1.63 to 14.3)	9999 (9999 to 9999)		
Day 253	4.96 (1.56 to 11.8)	1.45 (0.417 to 3.76)		
Day 281	4.96 (1.30 to 12.4)	9999 (9999 to 9999)		
Day 309	5.53 (1.74 to 11.6)	1.35 (0.195 to 2.77)		
Day 337	5.12 (2.17 to 10.5)	9999 (9999 to 9999)		
Day 365	4.50 (1.18 to 13.9)	1.45 (0.507 to 2.95)		
Day 393	3.10 (0.220 to 9.83)	9999 (9999 to 9999)		
Day 421	3.01 (0.239 to 9.54)	1.34 (0.325 to 2.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: CSF mHTT Protein Concentration Change in Geometric Mean (95%CI) from Baseline

End point title	CSF mHTT Protein Concentration Change in Geometric Mean (95%CI) from Baseline

End point description:

The results of the planned analysis related to mHTT protein levels in CSF are reported. Log (10) fmol/L changes in geometric mean (95%CI) were reported. Here "999" means that the values are not available (NA)

End point type	Secondary

End point timeframe:

From Baseline to Day 421

End point values	RO7234292 Monthly	RO7234292 Bimonthly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[2]	23[3]		
Units: Log (10) fmol/L				
geometric mean (confidence interval 95%)				
Day 29	-27.95 (-38.37 to -15.76)	-21.84 (-33.22 to -8.52)		
Day 57	-26.90 (-40.95 to -9.50)	10.11 (-41.68 to 107.88)		
Day 85	-50.30 (-59.00 to -39.75)	-32.63 (-44.31 to -18.50)		
Day 113	-49.13 (-58.77 to -37.18)	999 (999 to 999)		
Day 141	-54.02 (-61.05 to -45.72)	-41.76 (-50.59 to -31.35)		
Day 169	-42.33 (-53.66 to -28.23)	999 (999 to 999)		
Day 197	-40.79 (-52.59 to -26.05)	-36.48 (-48.99 to -20.89)		
Day 225	-47.01 (-58.69 to -32.02)	999 (999 to 999)		
Day 253	-43.63 (-55.39 to -28.77)	-41.06 (-53.19 to -25.78)		
Day 281	-40.29 (-58.63 to -13.80)	999 (999 to 999)		
Day 309	-36.67 (-50.11 to -19.60)	-40.82 (-52.37 to -26.46)		
Day 337	-42.71 (-58.93 to -20.07)	999 (999 to 999)		
Day 365	-49.55 (-62.02 to -32.98)	-55.07 (-65.46 to -41.57)		
Day 393	-41.55 (-59.46 to -15.74)	999 (999 to 999)		
Day 421	-45.45 (-56.21 to -32.03)	-41.51 (-52.22 to -28.39)		

Notes:

[2] - Only subjects for whom data were collected are included in the analysis.

[3] - Only subjects for whom data were collected are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change in Ventricular Volume Boundary Shift Integral from Baseline to 15 months

End point title	Mean Percentage Change in Ventricular Volume Boundary Shift Integral from Baseline to 15 months

End point description:

End point type	Secondary

End point timeframe:

Baseline up to 15 months

End point values	RO7234292 Monthly	RO7234292 Bimonthly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	18		
Units: Percentage				
arithmetic mean (standard deviation)	46.09 (± 32.14)	18.77 (± 10.36)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change in Caudate Volume Boundary Shift Integral from Baseline to 15 months

End point title	Mean Percentage Change in Caudate Volume Boundary Shift Integral from Baseline to 15 months

End point description:

End point type	Secondary

End point timeframe:

Baseline up to 15 months

End point values	RO7234292 Monthly	RO7234292 Bimonthly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	18		
Units: Percentage				
arithmetic mean (standard deviation)	8.64 (± 6.26)	5.67 (± 2.22)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change in Whole Brain Volume Boundary Shift Integral from Baseline to 15 months

End point title	Mean Percentage Change in Whole Brain Volume Boundary Shift Integral from Baseline to 15 months

End point description:

The numbers of analyzed subjects are lower than the actual subjects at that time point because some of the images did not pass quality review and data was lost.

End point type	Secondary

End point timeframe:

Baseline up to 15 months

End point values	RO7234292 Monthly	RO7234292 Bimonthly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	18		
Units: Percentage				
arithmetic mean (standard deviation)	1.63 (± 1.41)	0.89 (± 0.92)		

Statistical analyses

No statistical analyses for this end point

Secondary: EEG Parameters: Mean Change from Baseline to 15 Months in Absolute Power [8-12Hz]

End point title	EEG Parameters: Mean Change from Baseline to 15 Months in Absolute Power [8-12Hz]

End point description:

End point type	Secondary

End point timeframe:

Baseline to 15 Months

End point values	RO7234292 Monthly	RO7234292 Bimonthly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	19		
Units: log10(uV2)				
arithmetic mean (standard deviation)	0.11 (± 0.18)	0.02 (± 0.21)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Huntington's Disease Cognitive Assessment Battery Composite Score

End point title	Mean Change from Baseline in Huntington's Disease Cognitive Assessment Battery Composite Score

End point description:

Huntington's Disease Cognitive Assessment Battery Composite Score measures cognitive function. A positive change from baseline indicates improvement in cognitive function; a negative change indicates worsening in cognitive function.

End point type	Secondary

End point timeframe:

Baseline to 15 Months

End point values	RO7234292 Monthly	RO7234292 Bimonthly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	21		
Units: z-score				
arithmetic mean (standard deviation)				
Mean change from baseline	-0.33 (± 0.27)	-0.15 (± 0.23)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From baseline up to 1 year 9 months	
Adverse event reporting additional description:	
Safety population comprising all subjects that were randomized and received at least one dose of RO7234292	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups	
Reporting group title	RO7234292 Bimonthly
Reporting group description:	
RO7234292 was administered intrathecally every 56 days for 14 months following 2 monthly doses to serve as a loading dose.	
Reporting group title	RO7234292 Monthly
Reporting group description:	
RO7234292 was administered intrathecally every 28 days for 14 months.	

Serious adverse events	RO7234292 Bimonthly	RO7234292 Monthly	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 23 (13.04%)	4 / 23 (17.39%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 23 (4.35%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	1 / 23 (4.35%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	1 / 23 (4.35%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chest injury			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	1 / 23 (4.35%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis chemical			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column injury			
subjects affected / exposed	1 / 23 (4.35%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			

subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyporeflexia			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuritis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Suicide attempt			
subjects affected / exposed	1 / 23 (4.35%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Myelitis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	RO7234292 Bimonthly	RO7234292 Monthly	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 23 (95.65%)	22 / 23 (95.65%)	
Investigations			
CSF white blood cell count increased			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
CSF protein increased			
subjects affected / exposed	1 / 23 (4.35%)	2 / 23 (8.70%)	
occurrences (all)	1	3	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	12 / 23 (52.17%)	18 / 23 (78.26%)	
occurrences (all)	17	87	
Contusion			
subjects affected / exposed	5 / 23 (21.74%)	6 / 23 (26.09%)	
occurrences (all)	5	21	
Head injury			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Ligament sprain			
subjects affected / exposed	2 / 23 (8.70%)	1 / 23 (4.35%)	
occurrences (all)	2	1	
Limb injury			
subjects affected / exposed	0 / 23 (0.00%)	3 / 23 (13.04%)	
occurrences (all)	0	3	
Post lumbar puncture syndrome			
subjects affected / exposed	5 / 23 (21.74%)	4 / 23 (17.39%)	
occurrences (all)	6	10	
Skin abrasion			

subjects affected / exposed	4 / 23 (17.39%)	7 / 23 (30.43%)	
occurrences (all)	6	11	
Procedural pain			
subjects affected / exposed	12 / 23 (52.17%)	7 / 23 (30.43%)	
occurrences (all)	15	19	
Procedural headache			
subjects affected / exposed	2 / 23 (8.70%)	0 / 23 (0.00%)	
occurrences (all)	4	0	
Skin laceration			
subjects affected / exposed	3 / 23 (13.04%)	2 / 23 (8.70%)	
occurrences (all)	3	2	
Vascular disorders			
Haematoma			
subjects affected / exposed	2 / 23 (8.70%)	4 / 23 (17.39%)	
occurrences (all)	2	7	
Nervous system disorders			
Cerebral ventricle dilatation			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Balance disorder			
subjects affected / exposed	1 / 23 (4.35%)	3 / 23 (13.04%)	
occurrences (all)	1	3	
Dizziness			
subjects affected / exposed	2 / 23 (8.70%)	2 / 23 (8.70%)	
occurrences (all)	2	2	
Dysarthria			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	3	
Dyskinesia			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Headache			
subjects affected / exposed	4 / 23 (17.39%)	6 / 23 (26.09%)	
occurrences (all)	10	13	
Hyperkinesia			

subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Lumbar radiculopathy			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Motor dysfunction			
subjects affected / exposed	0 / 23 (0.00%)	3 / 23 (13.04%)	
occurrences (all)	0	3	
Parkinsonism			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Paraesthesia			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Presyncope			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Syncope			
subjects affected / exposed	2 / 23 (8.70%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 23 (4.35%)	3 / 23 (13.04%)	
occurrences (all)	1	3	
Gait disturbance			
subjects affected / exposed	0 / 23 (0.00%)	6 / 23 (26.09%)	
occurrences (all)	0	14	
Puncture site pain			
subjects affected / exposed	2 / 23 (8.70%)	2 / 23 (8.70%)	
occurrences (all)	4	3	
Injection site pain			
subjects affected / exposed	4 / 23 (17.39%)	2 / 23 (8.70%)	
occurrences (all)	4	3	
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 23 (21.74%)	0 / 23 (0.00%)	
occurrences (all)	6	0	
Nausea			
subjects affected / exposed	3 / 23 (13.04%)	3 / 23 (13.04%)	
occurrences (all)	5	3	
Vomiting			
subjects affected / exposed	2 / 23 (8.70%)	2 / 23 (8.70%)	
occurrences (all)	2	2	
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	2 / 23 (8.70%)	1 / 23 (4.35%)	
occurrences (all)	3	1	
Cough			
subjects affected / exposed	2 / 23 (8.70%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	3	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Irritability			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	3	
Insomnia			
subjects affected / exposed	2 / 23 (8.70%)	1 / 23 (4.35%)	
occurrences (all)	2	1	
Depression			

subjects affected / exposed	2 / 23 (8.70%)	4 / 23 (17.39%)	
occurrences (all)	2	4	
Depressed mood			
subjects affected / exposed	2 / 23 (8.70%)	2 / 23 (8.70%)	
occurrences (all)	2	2	
Tension			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 23 (8.70%)	3 / 23 (13.04%)	
occurrences (all)	2	4	
Pain in extremity			
subjects affected / exposed	2 / 23 (8.70%)	3 / 23 (13.04%)	
occurrences (all)	2	6	
Back pain			
subjects affected / exposed	4 / 23 (17.39%)	2 / 23 (8.70%)	
occurrences (all)	6	2	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 23 (4.35%)	2 / 23 (8.70%)	
occurrences (all)	1	2	
Ear infection			
subjects affected / exposed	0 / 23 (0.00%)	3 / 23 (13.04%)	
occurrences (all)	0	3	
Nasopharyngitis			
subjects affected / exposed	10 / 23 (43.48%)	9 / 23 (39.13%)	
occurrences (all)	15	14	
Upper respiratory tract infection			
subjects affected / exposed	1 / 23 (4.35%)	3 / 23 (13.04%)	
occurrences (all)	2	4	
Urinary tract infection			
subjects affected / exposed	2 / 23 (8.70%)	2 / 23 (8.70%)	
occurrences (all)	4	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 September 2017	Amendment 1 (Protocol version 2) made minor changes for consistency and to promote clarity prior to patient enrolment.
30 January 2018	Amendment 2 (Protocol version 3) changed the study design for the less frequent (quarterly, Q12W) dosing regimen to ensure that all study subjects would be exposed to a dose schedule that was predicted to be sufficient to provide clinical benefit if the drug acted as intended.
29 June 2018	Amendment 3 (Protocol version 4) included the option for the Sponsor to conduct one or more interim analyses to support internal decision-making on the overall RO7234292 clinical development program.
30 August 2018	Amendment 4 (Protocol version 5) reflected a change in sponsorship for the study and overall RO7234292 development from Ionis Pharmaceuticals, Inc. to F. Hoffmann-La Roche Ltd. and related updates to study drug name and manufacturer as well as to the assigned medical monitor. Provision was made for post-trial access to treatment through an OLE study BN40955 and for collection of subjects' HDID numbers to enable data from this study to be linked with data from other studies and registries.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported