Clinical trial results:
A Long-Term Follow-up Study Assessing the Safety and Efficacy of Vatelizumab in Multiple Sclerosis (MS) Patients Who Completed Treatment in Study DRI13839

Summary

EudraCT number	2014-003265-19
Trial protocol	PL
Global end of trial date	21 April 2016

Results information

Result version number	v1 (current)
This version publication date	22 July 2017
First version publication date	22 July 2017

Trial information

Trial identification

Sponsor protocol code	LTS13840

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02306811
WHO universal trial number (UTN)	U1111-1160-6120

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	500 Kendall Street, Cambridge, MA, United States, 02142
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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	02 November 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 April 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the long-term safety of vatelizumab in multiple sclerosis (MS) subjects.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial, the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi--Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 February 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Russian Federation: 29
Country: Number of subjects enrolled	United States: 11
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Poland: 20
Worldwide total number of subjects	62
EEA total number of subjects	20

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	62
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in 4 countries between 03 February 2015 and 21 April 2016. Subjects who completed 12-week treatment in the DRI13839 study (EudraCT no. 2014-001643-20) were offered to participate in this long-term study LTS13480.

Pre-assignment

Screening details:

Subjects who completed 12-week treatment for vatelizumab (1600 mg, 1200 mg, 800 mg or 400 mg) in DRI13839 study, continued on the same dose in the LTS13480 study and 24 subjects who completed 12-week treatment for placebo in DRI13839 study were randomized in 1:1:1:1 ratio to vatelizumab treatment groups (1600 mg, 1200 mg, 800 mg or 400 mg).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo to Vatelizumab (1600 mg, 1200 mg, 800 mg, or 400 mg)

Arm description:

Subjects who received placebo in DRI13839 study were randomized in 1:1:1:1 ratio to vatelizumab 1600 mg (6 subjects), vatelizumab 1200 mg (6 subjects), vatelizumab 800 mg (6 subjects) and vatelizumab 400 mg (6 subjects). Subjects received vatelizumab (1600 mg, 1200 mg, 800 mg or 400 mg) IV infusion once every 4 weeks for 96 weeks.

Arm type	Experimental
Investigational medicinal product name	Vatelizumab
Investigational medicinal product code	SAR339658
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion over a 60 minutes period.

Arm title	Vatelizumab 1600 mg

Arm description:

Vatelizumab 1600 mg IV infusion once every 4 weeks for 96 weeks.

Arm type	Experimental
Investigational medicinal product name	Vatelizumab
Investigational medicinal product code	SAR339658
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion over a 60 minutes period.

Arm title	Vatelizumab 1200 mg, 800 mg, or 400 mg

Arm description:

Vatelizumab 1200 mg, 800 mg or 400 mg IV infusion once every 4 weeks for 96 weeks.

Arm type	Experimental
Investigational medicinal product name	Vatelizumab
Investigational medicinal product code	SAR339658
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion over a 60 minutes period.

Number of subjects in period 1	Placebo to Vatelizumab (1600 mg, 1200 mg, 800 mg, or 400 mg)	Vatelizumab 1600 mg	Vatelizumab 1200 mg, 800 mg, or 400 mg
Started	24	27	11
Completed	0	0	0
Not completed	24	27	11
Consent withdrawn by subject	2	4	5
Study terminated by Sponsor	22	22	6
Other than specified	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo to Vatelizumab (1600 mg, 1200 mg, 800 mg, or 400 mg)

Reporting group description:

Subjects who received placebo in DRI13839 study were randomized in 1:1:1:1 ratio to vatelizumab 1600 mg (6 subjects), vatelizumab 1200 mg (6 subjects), vatelizumab 800 mg (6 subjects) and vatelizumab 400 mg (6 subjects). Subjects received vatelizumab (1600 mg, 1200 mg, 800 mg or 400 mg) IV infusion once every 4 weeks for 96 weeks.

Reporting group title	Vatelizumab 1600 mg

Reporting group description:

Vatelizumab 1600 mg IV infusion once every 4 weeks for 96 weeks.

Reporting group title	Vatelizumab 1200 mg, 800 mg, or 400 mg

Reporting group description:

Vatelizumab 1200 mg, 800 mg or 400 mg IV infusion once every 4 weeks for 96 weeks.

Reporting group values	Placebo to Vatelizumab (1600 mg, 1200 mg, 800 mg, or 400 mg)	Vatelizumab 1600 mg	Vatelizumab 1200 mg, 800 mg, or 400 mg
Number of subjects	24	27	11
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	39.3	33.8	37.1
standard deviation	± 9.56	± 10.12	± 8.38
Gender categorical			
Units: Subjects			
Female	19	15	6
Male	5	12	5

Reporting group values	Total		
Number of subjects	62		
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	40		
Male	22		

End points

End points reporting groups

Reporting group title	Placebo to Vatelizumab (1600 mg, 1200 mg, 800 mg, or 400 mg)

Reporting group description:

Subjects who received placebo in DRI13839 study were randomized in 1:1:1:1 ratio to vatelizumab 1600 mg (6 subjects), vatelizumab 1200 mg (6 subjects), vatelizumab 800 mg (6 subjects) and vatelizumab 400 mg (6 subjects). Subjects received vatelizumab (1600 mg, 1200 mg, 800 mg or 400 mg) IV infusion once every 4 weeks for 96 weeks.

Reporting group title	Vatelizumab 1600 mg

Reporting group description:

Vatelizumab 1600 mg IV infusion once every 4 weeks for 96 weeks.

Reporting group title	Vatelizumab 1200 mg, 800 mg, or 400 mg

Reporting group description:

Vatelizumab 1200 mg, 800 mg or 400 mg IV infusion once every 4 weeks for 96 weeks.

Primary: Percentage of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point title	Percentage of Subjects With Treatment Emergent Adverse Events (TEAEs)[1]

End point description:

Any untoward medical occurrence in subject who received study drug was considered an adverse event (AE) without regard to possibility of causal relationship with this treatment. TEAEs were defined as AEs that developed or worsened or became serious during on-treatment period (time from first administration of study drug to end of safety follow-up period [Week 192]). Serious adverse event (SAE) was defined as any untoward medical occurrence resulted in any of following: death, life-threatening, required initial or prolonged in-patient hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect, or considered as medically important event. Any TEAE included subjects with both serious and non-serious AEs. Related AEs were those related or possibly related by investigator and subjects were only counted once. Safety population:all subjects entered into study LTS13840 and analyzed based on treatment actually received.

End point type	Primary

End point timeframe:

From randomization up to end of study visit (Week 192)

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Placebo to Vatelizumab (1600 mg, 1200 mg, 800 mg, or 400 mg)	Vatelizumab 1600 mg	Vatelizumab 1200 mg, 800 mg, or 400 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	27	11	
Units: percentage of subjects				
number (not applicable)				
Any AE	62.5	37	36.4	
Related AE	8.3	14.8	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Brain Magnetic Resonance Imaging (MRI) Assessment: Cumulative Number of New Gadolinium Enhancing (Gd-enhancing) T1-lesions Per MRI Scan

End point title	Brain Magnetic Resonance Imaging (MRI) Assessment: Cumulative Number of New Gadolinium Enhancing (Gd-enhancing) T1-lesions Per MRI Scan

End point description:

Cumulative number of Gd-enhancing T1-lesions per scan were the total number of Gd-enhancing T1-lesions that occurred during the treatment period divided by the total number of scans performed during the treatment period. Analysis was performed on safety population. Here, 'n' signifies number of subjects with available data for specified timepoint and "99999" represents no subject analyzed at specified timepoint.

End point type	Secondary

End point timeframe:

Week 12, Week 32 and end of treatment (EOT) (maximum exposure: 225 days)

End point values	Placebo to Vatelizumab (1600 mg, 1200 mg, 800 mg, or 400 mg)	Vatelizumab 1600 mg	Vatelizumab 1200 mg, 800 mg, or 400 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	27	11	
Units: lesions per scan				
arithmetic mean (standard deviation)				
Week 12 (n= 19, 20, 0)	3.2 (± 5.32)	2.2 (± 4.64)	99999 (± 99999)	
Week 32 (n= 1, 0, 0)	0 (± 0)	99999 (± 99999)	99999 (± 99999)	
End of treatment (n= 5, 11, 3)	3.2 (± 2.17)	6.7 (± 10.82)	0 (± 0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Brain MRI Assessment: Cumulative Number of New or Newly Enlarging T2-lesions Per MRI Scan

End point title	Brain MRI Assessment: Cumulative Number of New or Newly Enlarging T2-lesions Per MRI Scan

End point description:

Cumulative number of new or newly enlarging T2-lesions per scan were the total number of new or newly enlarging T2-lesions that occurred during the treatment period divided by the total number of scans performed during the treatment period. Analysis was performed on safety population. Here, 'n' signifies number of subjects with available data for specified timepoint and "99999" represents no subject analyzed at specified timepoint.

End point type	Secondary

End point timeframe:

Week 12, Week 32 and EOT (maximum exposure: 225 days)

End point values	Placebo to Vatelizumab (1600 mg, 1200 mg, 800 mg, or 400 mg)	Vatelizumab 1600 mg	Vatelizumab 1200 mg, 800 mg, or 400 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	27	11	
Units: lesions per scan				
arithmetic mean (standard deviation)				
Week 12 (n= 19, 20, 0)	6.7 (± 10.62)	6.4 (± 9.08)	99999 (± 99999)	
Week 32 (n= 1, 0, 0)	3 (± 0)	99999 (± 99999)	99999 (± 99999)	
End of treatment (n= 5, 12, 3)	6.8 (± 4.32)	10.5 (± 17.7)	0.3 (± 0.58)	

Statistical analyses

No statistical analyses for this end point

Secondary: Blood Lymphocyte Sub-population Count: CD4+ Cells, CD8+ Cells, and CD19+ Cells

End point title	Blood Lymphocyte Sub-population Count: CD4+ Cells, CD8+ Cells, and CD19+ Cells

End point description:

Analysis was performed on pharmacokinetics/pharmacodynamics population that included all subjects who entered into and received at least 1 dose of investigational medicinal product (IMP) in the extension study LTS13840. Subjects were analyzed based on the treatment that they actually received. Here, 'n' signifies number of subjects with available data for specified timepoint.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Week 4, Week 100, Week 108

End point values	Placebo to Vatelizumab (1600 mg, 1200 mg, 800 mg, or 400 mg)	Vatelizumab 1600 mg	Vatelizumab 1200 mg, 800 mg, or 400 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	27	11	
Units: Cells count per micro liter				
arithmetic mean (standard deviation)				
CD4+ at Week 0 (n=24, 27, 11)	833.3 (± 242.54)	772.5 (± 277.73)	698.6 (± 286.22)	
CD4+ at Week 4 (n=20, 25, 8)	828.4 (± 269.13)	770.7 (± 295.43)	749.9 (± 178.83)	
CD4+ at Week 100 (n=22, 22, 7)	842.9 (± 284.7)	795.6 (± 324.71)	879 (± 247.72)	
CD4+ at Week 108 (n=20, 19, 6)	917.5 (± 472.95)	753.6 (± 410.34)	835.7 (± 294.01)	
CD8+ at Week 0 (n=24, 27, 11)	462.5 (± 199.24)	504.2 (± 202.59)	325.7 (± 137.98)	
CD8+ at Week 4 (n=20, 25, 8)	468.4 (± 201.26)	490.1 (± 172.96)	404.6 (± 123.09)	
CD8+ at Week 100 (n=22, 22, 7)	470.7 (± 214.43)	525.5 (± 221.58)	433.4 (± 142.59)	
CD8+ at Week 108 (n=20, 19, 6)	457.3 (± 206.29)	460.3 (± 195.58)	408.2 (± 151.07)	
CD19+ at Week 0 (n=24, 27, 11)	240.2 (± 116.34)	225.1 (± 87.32)	214.6 (± 114.49)	
CD19+ at Week 4 (n=20, 25, 8)	267.4 (± 178.91)	222 (± 103.61)	249.6 (± 126.38)	
CD19+ at Week 100 (n=22, 22, 7)	226.3 (± 95.26)	215.6 (± 96.08)	264.6 (± 108.75)	
CD19+ at Week 108 (n=20, 19, 6)	247.8 (± 137.49)	200.2 (± 80.79)	241 (± 137.86)	

Statistical analyses

No statistical analyses for this end point

Secondary: Blood Lymphocyte Sub-Population: CD4+/CD8+ Cells Ratio

End point title	Blood Lymphocyte Sub-Population: CD4+/CD8+ Cells Ratio

End point description:

Analysis was performed on pharmacokinetics/pharmacodynamics population. Subjects were analyzed based on the treatment that they actually received. Here, 'n' signifies number of subjects with available data for specified timepoint.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Week 4, Week 100, Week 108

End point values	Placebo to Vatelizumab (1600 mg, 1200 mg, 800 mg, or 400 mg)	Vatelizumab 1600 mg	Vatelizumab 1200 mg, 800 mg, or 400 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	27	11	
Units: ratio				
arithmetic mean (standard deviation)				
Week 0 (n=24, 27, 11)	2.1 (± 1.04)	1.7 (± 0.7)	2.3 (± 0.98)	
Week 4 (n=20, 25, 8)	2 (± 0.78)	1.7 (± 0.74)	2.1 (± 0.96)	
Week 100 (n=22, 22, 7)	2 (± 0.85)	1.7 (± 0.69)	2.2 (± 0.96)	
Week 108 (n=20, 18, 6)	2.1 (± 0.99)	1.8 (± 0.68)	2.2 (± 0.95)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics: Plasma Concentration of Vatelizumab

End point title	Pharmacokinetics: Plasma Concentration of Vatelizumab

End point description:

Blood samples were collected for determination of plasma vatelizumab concentration at Week 0, 4, 8 and 12 prior to the start of infusion and at the end of infusion. EOT data is for plasma level determinations that were performed at the time of early study termination (at time of Investigator decision to stop treatment or Sponsor decision to stop the study) and thus, represent different study visits/timepoints. Analysis was performed on safety population. Here, 'n' signifies number of subjects with available data for specified timepoints and and "99999" represents no subject analyzed at specified timepoint.

End point type	Secondary

End point timeframe:

Week 0, 4, 8 , 12 (pre-dose and any time after the end of infusion); Week 24, Week 96/EOT (pre-dose) and Week 100 (anytime)

End point values	Placebo to Vatelizumab (1600 mg, 1200 mg, 800 mg, or 400 mg)	Vatelizumab 1600 mg	Vatelizumab 1200 mg, 800 mg, or 400 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	27	11	
Units: mcg/mL				
arithmetic mean (standard deviation)				
Week 0: Predose (n=24,27,11)	0 (± 0)	118.1 (± 43.87)	65 (± 59.48)	
Week 0:after the end of infusion (n=22,24,10)	334.4 (± 148.75)	667.2 (± 171.74)	337.9 (± 169.88)	
Week 4:predose (n=21,25,8)	39.8 (± 28.11)	139 (± 47.2)	37.2 (± 30.44)	
Week 4:after the end of infusion (n=21,25,8)	388.3 (± 192.05)	656.5 (± 169.43)	278.7 (± 159.35)	

Week 8:predose (n=20,23,1)	52.5 (± 35.1)	132.3 (± 48.55)	53.8 (± 0)	
Week 8:after the end of infusion (n=20,23,1)	410.7 (± 202.16)	629.3 (± 166.64)	316.6 (± 0)	
Week 12: predose (n=19,20,0)	68.1 (± 52.81)	140.5 (± 53.84)	99999 (± 99999)	
Week 12:after the end of infusion (n=18,20,0)	415.8 (± 169.59)	681.2 (± 131.37)	99999 (± 99999)	
Week 24: predose (n=2,4,0)	103.4 (± 20.26)	99.1 (± 26.45)	99999 (± 99999)	
Week 96/EOT: predose (n=23,25,10)	76.5 (± 56.27)	144.2 (± 58.04)	49 (± 38.89)	
Week 100: (n=17,13,5)	20.9 (± 25.96)	39.6 (± 21.15)	13.7 (± 16.91)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were collected from signature of the informed consent form up to the final visit (Week 192) regardless of seriousness or relationship to study drug.

Adverse event reporting additional description:

Reported AEs are TEAEs that is AEs that developed/worsened during the 'on treatment period' (time from the first administration of study drug to the end of safety follow-up period [Week 192]).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Placebo to Vatelizumab (1600 mg, 1200 mg, 800 mg or 400 mg)

Reporting group description:

Subjects who received placebo in DRI13839 study were randomized in 1:1:1:1 ratio to vatelizumab 1600 mg (6 subjects), vatelizumab 1200 mg (6 subjects), vatelizumab 800 mg (6 subjects) and vatelizumab 400 mg (6 subjects). Subjects received vatelizumab (1600 mg, 1200 mg, 800 mg or 400 mg) IV infusion once every 4 weeks for 96 weeks.

Reporting group title	Vatelizumab 1600 mg

Reporting group description:

Vatelizumab 1600 mg IV infusion once every 4 weeks for 96 weeks.

Reporting group title	Vatelizumab 1200 mg, 800 mg or 400 mg

Reporting group description:

Vatelizumab 1200 mg, 800 mg or 400 mg IV infusion once every 4 weeks for 96 weeks.

Serious adverse events	Placebo to Vatelizumab (1600 mg, 1200 mg, 800 mg or 400 mg)	Vatelizumab 1600 mg	Vatelizumab 1200 mg, 800 mg or 400 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	1 / 27 (3.70%)	0 / 11 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Hepatobiliary disorders			
Hepatitis Acute			
subjects affected / exposed	0 / 24 (0.00%)	1 / 27 (3.70%)	0 / 11 (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
Infections and infestations			
Viral Infection			

subjects affected / exposed	1 / 24 (4.17%)	0 / 27 (0.00%)	0 / 11 (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	Placebo to Vatelizumab (1600 mg, 1200 mg, 800 mg or 400 mg)	Vatelizumab 1600 mg	Vatelizumab 1200 mg, 800 mg or 400 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 24 (45.83%)	6 / 27 (22.22%)	4 / 11 (36.36%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine Leiomyoma			
subjects affected / exposed	2 / 24 (8.33%)	0 / 27 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 24 (0.00%)	0 / 27 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	1 / 24 (4.17%)	3 / 27 (11.11%)	1 / 11 (9.09%)
occurrences (all)	1	5	1
Paraesthesia			
subjects affected / exposed	2 / 24 (8.33%)	0 / 27 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Sciatica			
subjects affected / exposed	0 / 24 (0.00%)	0 / 27 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 24 (8.33%)	0 / 27 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Fatigue			
subjects affected / exposed	1 / 24 (4.17%)	2 / 27 (7.41%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Pyrexia			

subjects affected / exposed	2 / 24 (8.33%)	1 / 27 (3.70%)	0 / 11 (0.00%)
occurrences (all)	3	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 24 (4.17%)	0 / 27 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 24 (0.00%)	0 / 27 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 24 (4.17%)	2 / 27 (7.41%)	0 / 11 (0.00%)
occurrences (all)	1	3	0
Upper Respiratory Tract Infection			
subjects affected / exposed	3 / 24 (12.50%)	0 / 27 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Urinary Tract Infection			
subjects affected / exposed	3 / 24 (12.50%)	0 / 27 (0.00%)	0 / 11 (0.00%)
occurrences (all)	5	0	0

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As per sponsor’s decision, study was discontinued in October 2015 based on planned interim analysis of the primary endpoint. However, subjects were followed up for safety monitoring. Decision for discontinuation was not linked to any safety concern.

Notes: