Clinical trial results:
An open-label study to evaluate the long-term safety and tolerability of AFQ056 in adolescent patients with Fragile X Syndrome

Summary

EudraCT number	2011-002379-40
Trial protocol	SE DE Outside EU/EEA GB ES DK IT FR NL BE
Global end of trial date	17 September 2014

Results information

Result version number	v1 (current)
This version publication date	13 April 2016
First version publication date	13 April 2016

Trial information

Trial identification

Sponsor protocol code	CAFQ056B2278

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01433354
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001003-PIP01-10
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 September 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 September 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the long-term safety and tolerability of AFQ056 in adolescent patients with FXS as assessed by:

Incidence and severity of adverse events and serious adverse events
Changes in vital signs, laboratory assessments, and ECGs
Monitoring the hypothalamic-pituitary-adrenal/thyroid axis function and childhood developmental milestones

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 November 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	United States: 47
Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Switzerland: 10
Worldwide total number of subjects	119
EEA total number of subjects	55

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)	105
Adults (18-64 years)	14
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 28 centres in 13 countries.

Pre-assignment

Screening details:

A total of 120 subjects were enrolled in the study, of which 119 subjects received study medication.

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:

As the study was an open-label study, this section was not applicable.

Arms

Arm title	AFQ056

Arm description:

Subjects treated with AFQ056 from a feeder study and entered the open-label extension study, were administered with AFQ056 capsule starting dose of 25 milligram (mg) twice daily (bid) and then titrated to 50 mg bid, 75 mg bid and 100 mg bid at weekly intervals.

Arm type	Experimental
Investigational medicinal product name	Mavoglurant
Investigational medicinal product code	AFQ056
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

AFQ056 (25 mg bid, 50 mg bid, 75 mg bid and 100 mg bid) was administered at weekly intervals.
25 mg bid = one 25 mg capsule taken twice a day
50 mg bid = two 25 mg capsules taken twice a day
75 mg bid = three 25 mg capsules taken twice a day
100 mg bid = one 100 mg capsule taken twice a day

Number of subjects in period 1	AFQ056
Started	119
Completed	0
Not completed	119
Consent withdrawn by subject	3
Adverse event, non-fatal	6
Administrative Problems	90
Lost to follow-up	1
Protocol deviation	2
Lack of efficacy	17

Baseline characteristics

Reporting groups	
Reporting group title	AFQ056
Reporting group description:	
Subjects treated with AFQ056 from a feeder study and entered the open-label extension study, were administered with AFQ056 capsule starting dose of 25 milligram (mg) twice daily (bid) and then titrated to 50 mg bid, 75 mg bid and 100 mg bid at weekly intervals.	

Reporting group values	AFQ056	Total	
Number of subjects	119	119	
Age categorical Units: Subjects			
12 to 19 years	119	119	
Age continuous Units: years arithmetic mean standard deviation	 15.2 ± 1.75	 -	
Gender categorical Units: Subjects			
Female Male	13 106	13 106	

Subject analysis sets	
Subject analysis set title	AFQ056 25 mg bid
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects were administered with AFQ056 25 mg bid during the open-label treatment period.	
Subject analysis set title	AFQ056 50 mg bid
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects were administered with AFQ056 50 mg bid during the open-label treatment period.	
Subject analysis set title	Prior to extension study first dose
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects were administered with AFQ056 during the core study and entered into the open-label treatment extension study.	
Subject analysis set title	AFQ056 100 mg bid
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects were administered with AFQ056 100 mg bid during the open-label treatment period	
Subject analysis set title	AFQ056 75 mg bid
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects were administered with AFQ056 75 mg bid during the open-label treatment period	
Subject analysis set title	Category 1
Subject analysis set type	Full analysis

Subject analysis set description:

Patients who entered into this open-label treatment study within one week of completion of Study CAFQ056B2214 or another study of AFQ056 which included FXS patients below 18 years of age were not required to undergo a screening visit. Patients entered the
study directly with the baseline (V2) visit as the first visit to be conducted. This baseline visit (V2) was conducted either during the same day with the last study visit of the previous study or at a different date but not more than one week apart.

Subject analysis set title	Category 2
Subject analysis set type	Full analysis

Subject analysis set description:

Patients who entered into this open-label treatment study from Study CAFQ056B2214 or Study CAFQ056B2131, or another study of AFQ056 which included FXS patients below 18 years of age could do so more than one week after completion of the last visit of the
respective previous study if any of the following reasons applied:
The patient discontinued the previous study due to lack of tolerability of the maximum dose in their assigned treatment group (entry into the extension trial could occur no sooner than the patient's originally-scheduled completion of the previous study)
The current open-label treatment study was pending health authority and/or ethics approval or other reasons prevented the patient from entering into this open-label treatment study earlier
unavailability of the current study when the patient completed the previous study

Reporting group values	AFQ056 25 mg bid	AFQ056 50 mg bid	Prior to extension study first dose
Number of subjects	119	118	31
Age categorical Units: Subjects			
12 to 19 years	119	118	31
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Gender categorical Units: Subjects			
Female Male			

Reporting group values	AFQ056 100 mg bid	AFQ056 75 mg bid	Category 1
Number of subjects	108	116	31
Age categorical Units: Subjects			
12 to 19 years	108	116	31
Age continuous Units: years arithmetic mean standard deviation	±	±	15.4 ± 1.61
Gender categorical Units: Subjects			
Female Male			

Reporting group values	Category 2		
Number of subjects	88		
Age categorical Units: Subjects			
12 to 19 years	88		

Age continuous Units: years arithmetic mean standard deviation	 15.1 ± 1.81		
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	AFQ056
Reporting group description:	
Subjects treated with AFQ056 from a feeder study and entered the open-label extension study, were administered with AFQ056 capsule starting dose of 25 milligram (mg) twice daily (bid) and then titrated to 50 mg bid, 75 mg bid and 100 mg bid at weekly intervals.	
Subject analysis set title	AFQ056 25 mg bid
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects were administered with AFQ056 25 mg bid during the open-label treatment period.	
Subject analysis set title	AFQ056 50 mg bid
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects were administered with AFQ056 50 mg bid during the open-label treatment period.	
Subject analysis set title	Prior to extension study first dose
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects were administered with AFQ056 during the core study and entered into the open-label treatment extension study.	
Subject analysis set title	AFQ056 100 mg bid
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects were administered with AFQ056 100 mg bid during the open-label treatment period	
Subject analysis set title	AFQ056 75 mg bid
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects were administered with AFQ056 75 mg bid during the open-label treatment period	
Subject analysis set title	Category 1
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients who entered into this open-label treatment study within one week of completion of Study CAFQ056B2214 or another study of AFQ056 which included FXS patients below 18 years of age were not required to undergo a screening visit. Patients entered the study directly with the baseline (V2) visit as the first visit to be conducted. This baseline visit (V2) was conducted either during the same day with the last study visit of the previous study or at a different date but not more than one week apart.	
Subject analysis set title	Category 2
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients who entered into this open-label treatment study from Study CAFQ056B2214 or Study CAFQ056B2131, or another study of AFQ056 which included FXS patients below 18 years of age could do so more than one week after completion of the last visit of the respective previous study if any of the following reasons applied: The patient discontinued the previous study due to lack of tolerability of the maximum dose in their assigned treatment group (entry into the extension trial could occur no sooner than the patient's originally-scheduled completion of the previous study) The current open-label treatment study was pending health authority and/or ethics approval or other reasons prevented the patient from entering into this open-label treatment study earlier unavailability of the current study when the patient completed the previous study	

Primary: Number of subjects with adverse events (AEs), treatment related AEs, AEs leading to discontinuation, AEs by severity, serious adverse events (SAEs) and SAEs leading to discontinuation during the study

End point title	Number of subjects with adverse events (AEs), treatment related AEs, AEs leading to discontinuation, AEs by severity, serious adverse events (SAEs) and SAEs leading to discontinuation during the study[1]

End point description:

Adverse events were summarized for the open-label treatment period, where the open-label treatment period is defined based on how AEs were collected and reported according to the manner in which patients entered the current study and which treatment (AFQ056 or placebo) they were receiving in the previous study.

AEs which were continuing from the core study or that started after the end of core study but prior to first dose of open-label study medication in the extension study for Category 1 patients ('Prior to Ext. first dose').

AEs which started during the open-label treatment period are presented based on the last AFQ056 dose taken on or before the onset date of the AE (25 mg bid; 50 mg bid; 75 mg bid; or 100 mg bid). No efficacy data presented as study was terminated.

End point type	Primary

End point timeframe:

Prior to first dose in extension study, Baseline (start of study treatment in extension study) to End of trial

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 summary statistics was planned for this outcome measure.

End point values	AFQ056	Prior to extension study first dose	AFQ056 25 mg bid	AFQ056 50 mg bid
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	119[2]	31[3]	119[4]	118[5]
Units: Number of subjects				
At least one AE	110	10	36	41
At least one severe AE	8	0	1	1
Any serious or significant AE	4	0	0	1
SAE	4	0	0	1
Discontinued due to AE	6	1	2	2
Discontinued due to SAE	1	0	0	0
Discontinued due to non serious AE	5	1	2	2

Notes:

[2] - Note: A patient can be counted or summarized in more than one dose column.

[3] - Note: A patient can be counted or summarized in more than one dose column.

[4] - Note: A patient can be counted or summarized in more than one dose column.

[5] - Note: A patient can be counted or summarized in more than one dose column.

End point values	AFQ056 75 mg bid	AFQ056 100 mg bid		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	116[6]	108[7]		
Units: Number of subjects				
At least one AE	44	90		
At least one severe AE	1	5		
Any serious or significant AE	0	3		
SAE	0	3		
Discontinued due to AE	0	3		
Discontinued due to SAE	0	1		

Discontinued due to non serious AE	0	2		

Notes:

[6] - Note: A patient can be counted or summarized in more than one dose column.

[7] - Note: A patient can be counted or summarized in more than one dose column.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Prior to Ext first dose
Reporting group description:	
Prior to Ext first dose	
Reporting group title	AFQ 25
Reporting group description:	
AFQ 25	
Reporting group title	AFQ 100
Reporting group description:	
AFQ 100	
Reporting group title	AFQ 75
Reporting group description:	
AFQ 75	
Reporting group title	Total
Reporting group description:	
Total	
Reporting group title	AFQ 50
Reporting group description:	
AFQ 50	

Serious adverse events	Prior to Ext first dose	AFQ 25	AFQ 100
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)	0 / 119 (0.00%)	3 / 108 (2.78%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	0 / 31 (0.00%)	0 / 119 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body			

subjects affected / exposed	0 / 31 (0.00%)	0 / 119 (0.00%)	0 / 108 (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 / 31 (0.00%)	0 / 119 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 119 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 119 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	AFQ 75	Total	AFQ 50
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 116 (0.00%)	4 / 119 (3.36%)	1 / 118 (0.85%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	0 / 116 (0.00%)	1 / 119 (0.84%)	0 / 118 (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
Foreign body			
subjects affected / exposed	0 / 116 (0.00%)	1 / 119 (0.84%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Aggression			

subjects affected / exposed	0 / 116 (0.00%)	1 / 119 (0.84%)	0 / 118 (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			
Appendicitis			
subjects affected / exposed	0 / 116 (0.00%)	1 / 119 (0.84%)	0 / 118 (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
Respiratory tract infection			
subjects affected / exposed	0 / 116 (0.00%)	1 / 119 (0.84%)	0 / 118 (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

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

Non-serious adverse events	Prior to Ext first dose	AFQ 25	AFQ 100
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 31 (19.35%)	23 / 119 (19.33%)	74 / 108 (68.52%)
Investigations			
Weight increased			
subjects affected / exposed	1 / 31 (3.23%)	1 / 119 (0.84%)	5 / 108 (4.63%)
occurrences (all)	1	1	5
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 31 (0.00%)	4 / 119 (3.36%)	8 / 108 (7.41%)
occurrences (all)	0	5	8
Psychomotor hyperactivity			
subjects affected / exposed	0 / 31 (0.00%)	2 / 119 (1.68%)	3 / 108 (2.78%)
occurrences (all)	0	2	3
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 31 (0.00%)	2 / 119 (1.68%)	5 / 108 (4.63%)
occurrences (all)	0	2	5
Pyrexia			

subjects affected / exposed	0 / 31 (0.00%)	0 / 119 (0.00%)	4 / 108 (3.70%)
occurrences (all)	0	0	7
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 31 (3.23%)	2 / 119 (1.68%)	8 / 108 (7.41%)
occurrences (all)	1	2	14
Diarrhoea			
subjects affected / exposed	1 / 31 (3.23%)	2 / 119 (1.68%)	5 / 108 (4.63%)
occurrences (all)	1	2	6
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 31 (0.00%)	1 / 119 (0.84%)	7 / 108 (6.48%)
occurrences (all)	0	1	9
Epistaxis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 119 (0.00%)	3 / 108 (2.78%)
occurrences (all)	0	0	6
Psychiatric disorders			
Aggression			
subjects affected / exposed	0 / 31 (0.00%)	3 / 119 (2.52%)	12 / 108 (11.11%)
occurrences (all)	0	4	22
Agitation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 119 (0.84%)	4 / 108 (3.70%)
occurrences (all)	0	1	5
Anxiety			
subjects affected / exposed	0 / 31 (0.00%)	3 / 119 (2.52%)	11 / 108 (10.19%)
occurrences (all)	0	3	12
Initial insomnia			
subjects affected / exposed	0 / 31 (0.00%)	3 / 119 (2.52%)	9 / 108 (8.33%)
occurrences (all)	0	3	9
Insomnia			
subjects affected / exposed	1 / 31 (3.23%)	4 / 119 (3.36%)	12 / 108 (11.11%)
occurrences (all)	1	4	12
Irritability			
subjects affected / exposed	0 / 31 (0.00%)	3 / 119 (2.52%)	9 / 108 (8.33%)
occurrences (all)	0	3	9
Infections and infestations			

Ear infection			
subjects affected / exposed	0 / 31 (0.00%)	2 / 119 (1.68%)	5 / 108 (4.63%)
occurrences (all)	0	2	6
Gastroenteritis viral			
subjects affected / exposed	0 / 31 (0.00%)	0 / 119 (0.00%)	5 / 108 (4.63%)
occurrences (all)	0	0	6
Influenza			
subjects affected / exposed	0 / 31 (0.00%)	1 / 119 (0.84%)	6 / 108 (5.56%)
occurrences (all)	0	1	6
Upper respiratory tract infection			
subjects affected / exposed	1 / 31 (3.23%)	3 / 119 (2.52%)	9 / 108 (8.33%)
occurrences (all)	1	6	12
Nasopharyngitis			
subjects affected / exposed	0 / 31 (0.00%)	7 / 119 (5.88%)	25 / 108 (23.15%)
occurrences (all)	0	7	34
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 31 (6.45%)	0 / 119 (0.00%)	0 / 108 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	AFQ 75	Total	AFQ 50
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 116 (29.31%)	103 / 119 (86.55%)	30 / 118 (25.42%)
Investigations			
Weight increased			
subjects affected / exposed	0 / 116 (0.00%)	7 / 119 (5.88%)	0 / 118 (0.00%)
occurrences (all)	0	7	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 116 (3.45%)	15 / 119 (12.61%)	1 / 118 (0.85%)
occurrences (all)	5	19	1
Psychomotor hyperactivity			
subjects affected / exposed	1 / 116 (0.86%)	9 / 119 (7.56%)	3 / 118 (2.54%)
occurrences (all)	1	9	3
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	3 / 116 (2.59%)	11 / 119 (9.24%)	2 / 118 (1.69%)
occurrences (all)	3	12	2
Pyrexia			
subjects affected / exposed	2 / 116 (1.72%)	7 / 119 (5.88%)	1 / 118 (0.85%)
occurrences (all)	5	13	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 116 (0.00%)	13 / 119 (10.92%)	5 / 118 (4.24%)
occurrences (all)	0	22	5
Diarrhoea			
subjects affected / exposed	1 / 116 (0.86%)	12 / 119 (10.08%)	4 / 118 (3.39%)
occurrences (all)	1	14	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 116 (3.45%)	12 / 119 (10.08%)	1 / 118 (0.85%)
occurrences (all)	4	15	1
Epistaxis			
subjects affected / exposed	2 / 116 (1.72%)	6 / 119 (5.04%)	2 / 118 (1.69%)
occurrences (all)	2	10	2
Psychiatric disorders			
Aggression			
subjects affected / exposed	4 / 116 (3.45%)	19 / 119 (15.97%)	3 / 118 (2.54%)
occurrences (all)	8	36	3
Agitation			
subjects affected / exposed	0 / 116 (0.00%)	6 / 119 (5.04%)	1 / 118 (0.85%)
occurrences (all)	0	8	2
Anxiety			
subjects affected / exposed	0 / 116 (0.00%)	15 / 119 (12.61%)	1 / 118 (0.85%)
occurrences (all)	0	16	1
Initial insomnia			
subjects affected / exposed	4 / 116 (3.45%)	18 / 119 (15.13%)	2 / 118 (1.69%)
occurrences (all)	6	20	2
Insomnia			
subjects affected / exposed	5 / 116 (4.31%)	25 / 119 (21.01%)	10 / 118 (8.47%)
occurrences (all)	5	31	10
Irritability			

subjects affected / exposed	3 / 116 (2.59%)	15 / 119 (12.61%)	1 / 118 (0.85%)
occurrences (all)	4	17	1
Infections and infestations			
Ear infection			
subjects affected / exposed	1 / 116 (0.86%)	8 / 119 (6.72%)	0 / 118 (0.00%)
occurrences (all)	1	9	0
Gastroenteritis viral			
subjects affected / exposed	1 / 116 (0.86%)	8 / 119 (6.72%)	2 / 118 (1.69%)
occurrences (all)	1	9	2
Influenza			
subjects affected / exposed	2 / 116 (1.72%)	8 / 119 (6.72%)	0 / 118 (0.00%)
occurrences (all)	2	9	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 116 (2.59%)	17 / 119 (14.29%)	5 / 118 (4.24%)
occurrences (all)	3	28	6
Nasopharyngitis			
subjects affected / exposed	8 / 116 (6.90%)	35 / 119 (29.41%)	3 / 118 (2.54%)
occurrences (all)	9	55	5
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 116 (0.86%)	5 / 119 (4.20%)	2 / 118 (1.69%)
occurrences (all)	1	5	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 October 2011	Modified the inclusion criteria with respect to enrolment of female subjects of childbearing potential had to undergo additional pregnancy testing.
13 August 2013	The criteria for liver safety monitoring was included to ensure the safety and to determine the hepatotoxic potential of investigational drug. The description and use of the ABC-CFX scoring algorithm was added throughout the protocol. Changes were made throughout the protocol related to the optional testing to determine the extent of methylation of the FMR1 gene. Changes were made throughout the protocol to allow the possibility for eligible subjects from other studies of AFQ056. An instruction for subjects to avoid drinking grapefruit juice was added to exclusion criterion.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The sponsor decided to terminate the study, as the study treatment, AFQ056, failed to demonstrate efficacy in target population in two other clinical studies.

Notes: