



Clinical trial results:

An open-label treatment study to evaluate the safety, tolerability and efficacy of AFQ056 in Parkinson's patients with L-dopa induced dyskinesias

Summary

EudraCT number	2010-019418-25
Trial protocol	IT FR DE FI
Global end of trial date	15 October 2013

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	03 August 2015

Trial information

Trial identification

Sponsor protocol code	CAFQ056A2217
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01173731
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)	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	15 October 2013
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	15 October 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary objectives: To evaluate the safety and tolerability of AFQ056 in patients with PD-LID as assessed by: • Incidence and severity of adverse events and serious adverse events • Changes in vital signs, laboratory assessments, and ECGs • Changes in cognitive function as measured by the MMSE • Changes in psychiatric symptoms as measured by the SCOPA-PC • Changes in underlying symptoms of PD as measured by the UPDRS part III and the PD symptom items in the Clinical Global Impression of Change (CGIC) and Patient Global Impression of Change (PGIC), and by AEs potentially related to an exacerbation of movement disorder of PD • Occurrence of rebound symptoms upon discontinuation of study drug

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 October 2010
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	Germany: 26
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	France: 5
Worldwide total number of subjects	66
EEA total number of subjects	45

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	31
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study population consisted of male or female patients with PD-L1D who have completed selected double-blind studies with AFQ056 or placebo.

Period 1

Period 1 title	Open-label Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	AFQ056 10 mg b.i.d.

Arm description:

The investigational drug, AFQ056, was provided as hard gelatin capsules.

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

Dosage and administration details:

Patients were asked to take the number of capsules in the morning and in the evening as indicated. The morning and evening doses were taken at approximately 12-hour intervals. If a patient missed a dose of study drug for any reason, the patient was instructed to not make up the missed dose with the next scheduled dose. Study drug was administered with a glass of water. Patients were instructed to not chew the medication, but swallow it whole. Patients were asked to avoid drinking grapefruit juice during the study.

Arm title	AFQ056 25 mg b.i.d
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Arm description:

The investigational drug, AFQ056, was provided as hard gelatin capsules.

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

Dosage and administration details:

Patients were asked to take the number of capsules in the morning and in the evening as indicated. The morning and evening doses were taken at approximately 12-hour intervals. If a patient missed a dose of study drug for any reason, the patient was instructed to not make up the missed dose with the next scheduled dose. Study drug was administered with a glass of water. Patients were instructed to not chew the medication, but swallow it whole. Patients were asked to avoid drinking grapefruit juice during the study.

Arm title	AFQ056 50 mg b.i.d.
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Arm description:

The investigational drug, AFQ056, was provided as hard gelatin capsules.

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

Dosage and administration details:

Patients were asked to take the number of capsules in the morning and in the evening as indicated. The morning and evening doses were taken at approximately 12-hour intervals. If a patient missed a dose of study drug for any reason, the patient was instructed to not make up the missed dose with the next scheduled dose. Study drug was administered with a glass of water. Patients were instructed to not chew the medication, but swallow it whole. Patients were asked to avoid drinking grapefruit juice during the study.

Arm title	AFQ056 75 mg b.i.d.
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Arm description:

The investigational drug, AFQ056, was provided as hard gelatin capsules.

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

Dosage and administration details:

Patients were asked to take the number of capsules in the morning and in the evening as indicated. The morning and evening doses were taken at approximately 12-hour intervals. If a patient missed a dose of study drug for any reason, the patient was instructed to not make up the missed dose with the next scheduled dose. Study drug was administered with a glass of water. Patients were instructed to not chew the medication, but swallow it whole. Patients were asked to avoid drinking grapefruit juice during the study.

Arm title	AFQ056 100 mg b.i.d
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Arm description:

The investigational drug, AFQ056, was provided as hard gelatin capsules.

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

Dosage and administration details:

Patients were asked to take the number of capsules in the morning and in the evening as indicated. The morning and evening doses were taken at approximately 12-hour intervals. If a patient missed a dose of study drug for any reason, the patient was instructed to not make up the missed dose with the next scheduled dose. Study drug was administered with a glass of water. Patients were instructed to not chew the medication, but swallow it whole. Patients were asked to avoid drinking grapefruit juice during the study.

Number of subjects in period 1	AFQ056 10 mg b.i.d.	AFQ056 25 mg b.i.d	AFQ056 50 mg b.i.d.
Started	3	16	13
Completed	0	0	0
Not completed	3	16	13
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	1	-	3

Unsatisfactory therapeutic effect	1	1	4
Administrative problems	-	5	3
Adverse Event(s)	1	8	3
Lost to follow-up	-	1	-

Number of subjects in period 1	AFQ056 75 mg b.i.d.	AFQ056 100 mg b.i.d
Started	15	19
Completed	0	0
Not completed	15	19
Adverse event, serious fatal	1	-
Consent withdrawn by subject	1	4
Unsatisfactory therapeutic effect	2	5
Administrative problems	3	5
Adverse Event(s)	8	5
Lost to follow-up	-	-

Baseline characteristics

Reporting groups

Reporting group title	AFQ056 10 mg b.i.d.
Reporting group description: The investigational drug, AFQ056, was provided as hard gelatin capsules.	
Reporting group title	AFQ056 25 mg b.i.d
Reporting group description: The investigational drug, AFQ056, was provided as hard gelatin capsules.	
Reporting group title	AFQ056 50 mg b.i.d.
Reporting group description: The investigational drug, AFQ056, was provided as hard gelatin capsules.	
Reporting group title	AFQ056 75 mg b.i.d.
Reporting group description: The investigational drug, AFQ056, was provided as hard gelatin capsules.	
Reporting group title	AFQ056 100 mg b.i.d
Reporting group description: The investigational drug, AFQ056, was provided as hard gelatin capsules.	

Reporting group values	AFQ056 10 mg b.i.d.	AFQ056 25 mg b.i.d	AFQ056 50 mg b.i.d.
Number of subjects	3	16	13
Age categorical Units: Subjects			
Adults (18-64 years)	1	9	4
From 65-84 years	2	7	9
Age continuous Units: years			
arithmetic mean	64.7	63.3	65.5
standard deviation	± 14.5	± 6.82	± 6.42
Gender categorical Units: Subjects			
Female	1	13	6
Male	2	3	7

Reporting group values	AFQ056 75 mg b.i.d.	AFQ056 100 mg b.i.d	Total
Number of subjects	15	19	66
Age categorical Units: Subjects			
Adults (18-64 years)	7	10	31
From 65-84 years	8	9	35
Age continuous Units: years			
arithmetic mean	62.6	64.2	-
standard deviation	± 9.09	± 6.88	-
Gender categorical Units: Subjects			
Female	5	9	34
Male	10	10	32

Subject analysis sets

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS included all patients who received at least one dose of open-label study medication during this open-label study.

Subject analysis set title	Safety Set (SS)
Subject analysis set type	Safety analysis

Subject analysis set description:

The SS consisted of all patients who received at least one dose of open-label study medication during this open-label study and who had at least one post-baseline safety assessment.

Reporting group values	Full Analysis Set (FAS)	Safety Set (SS)	
Number of subjects	66	66	
Age categorical Units: Subjects			
Adults (18-64 years)	31	31	
From 65-84 years	35	35	
Age continuous Units: years arithmetic mean standard deviation	\pm	\pm	
Gender categorical Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	AFQ056 10 mg b.i.d.
Reporting group description: The investigational drug, AFQ056, was provided as hard gelatin capsules.	
Reporting group title	AFQ056 25 mg b.i.d.
Reporting group description: The investigational drug, AFQ056, was provided as hard gelatin capsules.	
Reporting group title	AFQ056 50 mg b.i.d.
Reporting group description: The investigational drug, AFQ056, was provided as hard gelatin capsules.	
Reporting group title	AFQ056 75 mg b.i.d.
Reporting group description: The investigational drug, AFQ056, was provided as hard gelatin capsules.	
Reporting group title	AFQ056 100 mg b.i.d.
Reporting group description: The investigational drug, AFQ056, was provided as hard gelatin capsules.	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description: The FAS included all patients who received at least one dose of open-label study medication during this open-label study.	
Subject analysis set title	Safety Set (SS)
Subject analysis set type	Safety analysis
Subject analysis set description: The SS consisted of all patients who received at least one dose of open-label study medication during this open-label study and who had at least one post-baseline safety assessment.	

Primary: Changes from baseline in cognitive function as measured by the Mini-Mental State Examination (MMSE) total score

End point title	Changes from baseline in cognitive function as measured by the Mini-Mental State Examination (MMSE) total score ^[1]
End point description: The study was terminated based on the results of studies CAFQ056A2222 and CAFQ056A2223 (due to lack of efficacy) and the sponsor's decision to terminate the program.	
End point type	Primary
End point timeframe: Baseline through Month 36	

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: No statistical analyses have been performed for this primary end point.

End point values	Safety Set (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	0 ^[2]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Month 6 baseline	()			
Month 6 change from baseline	()			

Month 12 baseline	()			
Month 12 change from baseline	()			
Month 18 baseline	()			
Month 18 change from baseline	()			
Month 24 baseline	()			
Month 24 change from baseline	()			
Month 30 baseline	()			
Month 30 change from baseline	()			
Month 36 baseline	()			
Month 36 change from baseline	()			

Notes:

[2] - The study was terminated based on the results of studies CAFQ056A2222 and CAFQ056A2223 (due to lack

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.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	AFQ056 10mg
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Reporting group description:

AFQ056 10mg

Reporting group title	AFQ056 25mg
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Reporting group description:

AFQ056 25mg

Reporting group title	AFQ056 100mg
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Reporting group description:

AFQ056 100mg

Reporting group title	AFQ056 75mg
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Reporting group description:

AFQ056 75mg

Reporting group title	AFQ056 50mg
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Reporting group description:

AFQ056 50mg

Serious adverse events	AFQ056 10mg	AFQ056 25mg	AFQ056 100mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	4 / 16 (25.00%)	8 / 19 (42.11%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Meningioma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Prostate cancer			

subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
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, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (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 arrest			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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			
Delusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination, visual			

subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (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
Laceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Limb injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (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
Meniscus injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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

Radius fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Road traffic accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sternal fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Toxicity to various agents			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Ulna fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
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			
Cardiac arrest			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (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
Nervous system disorders			
Akinesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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

Balance disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Cognitive disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Freezing phenomenon			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
On and off phenomenon			
subjects affected / exposed	1 / 3 (33.33%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinson's disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Thoracic outlet syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Gastroesophageal reflux disease subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus bladder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (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
Fracture pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Lumbar spinal stenosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Rotator cuff syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Arthritis infective			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumococcal sepsis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
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	AFQ056 75mg	AFQ056 50mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 15 (53.33%)	4 / 13 (30.77%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Meningioma			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			

subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delusion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination, visual			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			

subjects affected / exposed	0 / 15 (0.00%)	2 / 13 (15.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sternal fracture			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			

subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	2 / 15 (13.33%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Akinesia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balance disorder			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Freezing phenomenon			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxic-ischaemic encephalopathy			

subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
On and off phenomenon			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson's disease			
subjects affected / exposed	2 / 15 (13.33%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic outlet syndrome			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus bladder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			

subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Arthritis infective			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	AFQ056 10mg	AFQ056 25mg	AFQ056 100mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	16 / 16 (100.00%)	17 / 19 (89.47%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Eyelid tumour			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Orthostatic hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	3 / 19 (15.79%)
occurrences (all)	0	0	3
Feeling abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1

Gait disturbance subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	2 / 19 (10.53%) 2
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Reproductive system and breast disorders Ejaculation disorder subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Allergic cough subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Cough subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 16 (6.25%) 1	2 / 19 (10.53%) 2
Epistaxis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 16 (6.25%) 2	1 / 19 (5.26%) 1
Hyperventilation subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Psychiatric disorders Abnormal behaviour subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Acute psychosis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Abnormal dreams			
subjects affected / exposed	0 / 3 (0.00%)	3 / 16 (18.75%)	2 / 19 (10.53%)
occurrences (all)	0	4	3
Aggression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Agitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Compulsive shopping			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Depersonalisation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Delusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 3 (0.00%)	2 / 16 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Hallucination, visual			
subjects affected / exposed	0 / 3 (0.00%)	3 / 16 (18.75%)	3 / 19 (15.79%)
occurrences (all)	0	3	4
Hallucination, auditory			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hallucinations, mixed			

subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Impulsive behaviour			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Illusion			
subjects affected / exposed	0 / 3 (0.00%)	2 / 16 (12.50%)	1 / 19 (5.26%)
occurrences (all)	0	3	1
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 16 (0.00%)	5 / 19 (26.32%)
occurrences (all)	1	0	5
Jealous delusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Nightmare			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Libido increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Panic attack			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Pathological gambling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Investigations			
Amylase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	3
Blood fibrinogen increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Blood magnesium decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Blood pressure increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Fibrin D dimer increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Haemoglobin decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	3 / 19 (15.79%)
occurrences (all)	0	0	3
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1

Mean cell haemoglobin concentration decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Neutrophil count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Red blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	3 / 19 (15.79%)
occurrences (all)	0	0	3
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
White blood cells urine positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	2 / 19 (10.53%)
occurrences (all)	0	1	2
Fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Laceration			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Incisional hernia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Tendon rupture subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Wound subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0
Cardiac disorders Acute myocardial infarction subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Arrhythmia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0
Atrial fibrillation subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Atrioventricular block first degree subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Nervous system disorders Akinesia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	4 / 16 (25.00%) 4	0 / 19 (0.00%) 0
Bradykinesia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Cognitive disorder subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Carpal tunnel syndrome			

subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Coordination abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Depressed level of consciousness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	1 / 3 (33.33%)	1 / 16 (6.25%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	2 / 16 (12.50%)	4 / 19 (21.05%)
occurrences (all)	0	4	4
Dysarthria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dyskinesia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 16 (18.75%)	3 / 19 (15.79%)
occurrences (all)	0	3	5
Dystonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	3 / 16 (18.75%)	3 / 19 (15.79%)
occurrences (all)	0	5	3
Freezing phenomenon			
subjects affected / exposed	0 / 3 (0.00%)	2 / 16 (12.50%)	2 / 19 (10.53%)
occurrences (all)	0	2	4
Hyperkinesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hypersomnia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 16 (12.50%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Memory impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Motor dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
On and off phenomenon			
subjects affected / exposed	2 / 3 (66.67%)	2 / 16 (12.50%)	6 / 19 (31.58%)
occurrences (all)	2	2	9
Paraesthesia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Parkinson's disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Sensory disturbance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)	4 / 16 (25.00%)	2 / 19 (10.53%)
occurrences (all)	0	4	2
Speech disorder			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Stupor subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Blood and lymphatic system disorders			
Bicytopenia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Anaemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 16 (12.50%) 2	0 / 19 (0.00%) 0
Leukopenia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0
Eosinophilia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Ear and labyrinth disorders			
Tinnitus subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Vertigo subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 16 (6.25%) 2	0 / 19 (0.00%) 0
Eye disorders			
Altered visual depth perception subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Cataract subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Diplopia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	2 / 16 (12.50%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Visual impairment			
subjects affected / exposed	0 / 3 (0.00%)	2 / 16 (12.50%)	2 / 19 (10.53%)
occurrences (all)	0	2	2
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 3 (33.33%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	3 / 19 (15.79%)
occurrences (all)	0	0	3
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dental caries			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gastrointestinal hypermotility			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Nausea subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	2 / 16 (12.50%) 2	1 / 19 (5.26%) 1
Hypoaesthesia oral subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0
Paraesthesia oral subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 16 (0.00%) 0	2 / 19 (10.53%) 2
Skin and subcutaneous tissue disorders			
Pruritus subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Onycholysis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Alopecia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Rash subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Skin discolouration subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Renal and urinary disorders			
Micturition urgency subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	0 / 19 (0.00%) 0
Pollakiuria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Renal failure			

subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Renal failure chronic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Urge incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Bursitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Fracture pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Mobility decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Osteoarthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rotator cuff syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	2 / 16 (12.50%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Spinal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Trigger finger			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0

Folliculitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 16 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	3	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pulpitis dental			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Sialoadenitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Tracheitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	3 / 19 (15.79%)
occurrences (all)	0	1	3
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Urosepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hypercholesterolaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	AFQ056 75mg	AFQ056 50mg	
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	15 / 15 (100.00%)	13 / 13 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Eyelid tumour			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 15 (13.33%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Hypotension			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Orthostatic hypotension			
subjects affected / exposed	2 / 15 (13.33%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Fatigue			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Feeling abnormal			
subjects affected / exposed	2 / 15 (13.33%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Feeling hot			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Gait disturbance			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 13 (7.69%) 1	
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	2 / 13 (15.38%) 2	
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	
Reproductive system and breast disorders Ejaculation disorder subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 13 (7.69%) 1	
Respiratory, thoracic and mediastinal disorders Allergic cough subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Cough subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 13 (7.69%) 1	
Dyspnoea subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Epistaxis subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 4	0 / 13 (0.00%) 0	
Hyperventilation subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Psychiatric disorders Abnormal behaviour subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Acute psychosis subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	

Abnormal dreams		
subjects affected / exposed	2 / 15 (13.33%)	0 / 13 (0.00%)
occurrences (all)	3	0
Aggression		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Agitation		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Anxiety		
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	1
Confusional state		
subjects affected / exposed	1 / 15 (6.67%)	1 / 13 (7.69%)
occurrences (all)	1	1
Compulsive shopping		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Depersonalisation		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Delusion		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Depression		
subjects affected / exposed	3 / 15 (20.00%)	1 / 13 (7.69%)
occurrences (all)	3	2
Hallucination, visual		
subjects affected / exposed	2 / 15 (13.33%)	1 / 13 (7.69%)
occurrences (all)	3	1
Hallucination, auditory		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Hallucinations, mixed		
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	1

Impulsive behaviour subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	
Illusion subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2	1 / 13 (7.69%) 1	
Insomnia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 13 (7.69%) 1	
Jealous delusion subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2	0 / 13 (0.00%) 0	
Nightmare subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Libido increased subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2	0 / 13 (0.00%) 0	
Panic attack subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Pathological gambling subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	
Sleep disorder subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	
Investigations			
Amylase increased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2	0 / 13 (0.00%) 0	
Blood creatinine increased			

subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Blood fibrinogen increased		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Blood lactate dehydrogenase increased		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Blood magnesium decreased		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Blood pressure increased		
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	2
Blood urea increased		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Fibrin D dimer increased		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Cardiac murmur		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Haemoglobin decreased		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Lipase increased		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Lymphocyte count decreased		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Mean cell haemoglobin concentration decreased		

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Neutrophil count increased subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	
Platelet count decreased subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	
Red blood cell count decreased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Weight decreased subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	2 / 13 (15.38%) 2	
White blood cell count decreased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Weight increased subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	
White blood cells urine positive subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Fall subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	3 / 13 (23.08%) 7	
Fracture subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 13 (7.69%) 1	
Laceration			

subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Incisional hernia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Tendon rupture			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Wound			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Arrhythmia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Atrial fibrillation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Atrioventricular block first degree			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Akinesia			
subjects affected / exposed	3 / 15 (20.00%)	1 / 13 (7.69%)	
occurrences (all)	3	1	
Bradykinesia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Cognitive disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Carpal tunnel syndrome			

subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Coordination abnormal		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Depressed level of consciousness		
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	1
Disturbance in attention		
subjects affected / exposed	2 / 15 (13.33%)	0 / 13 (0.00%)
occurrences (all)	2	0
Dizziness		
subjects affected / exposed	6 / 15 (40.00%)	5 / 13 (38.46%)
occurrences (all)	8	5
Dysarthria		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Dysgeusia		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Dyskinesia		
subjects affected / exposed	3 / 15 (20.00%)	2 / 13 (15.38%)
occurrences (all)	3	2
Dystonia		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Headache		
subjects affected / exposed	3 / 15 (20.00%)	1 / 13 (7.69%)
occurrences (all)	3	1
Freezing phenomenon		
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	1
Hyperkinesia		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Hypersomnia		

subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Hypoaesthesia		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Memory impairment		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Motor dysfunction		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
On and off phenomenon		
subjects affected / exposed	2 / 15 (13.33%)	1 / 13 (7.69%)
occurrences (all)	2	1
Paraesthesia		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Parkinson's disease		
subjects affected / exposed	5 / 15 (33.33%)	2 / 13 (15.38%)
occurrences (all)	5	4
Sciatica		
subjects affected / exposed	1 / 15 (6.67%)	1 / 13 (7.69%)
occurrences (all)	1	1
Restless legs syndrome		
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	1
Presyncope		
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	1
Sensory disturbance		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Somnolence		
subjects affected / exposed	1 / 15 (6.67%)	2 / 13 (15.38%)
occurrences (all)	1	2
Speech disorder		

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Stupor subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 13 (7.69%) 1	
Syncope subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Blood and lymphatic system disorders			
Bicytopenia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	
Anaemia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Leukopenia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Eosinophilia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 13 (7.69%) 1	
Ear and labyrinth disorders			
Tinnitus subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2	0 / 13 (0.00%) 0	
Vertigo subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Eye disorders			
Altered visual depth perception subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 13 (7.69%) 1	
Cataract subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 13 (7.69%) 2	
Diplopia			

subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Photophobia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Vision blurred			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Visual impairment			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Dental caries			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Flatulence			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Dry mouth			
subjects affected / exposed	2 / 15 (13.33%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal hypermotility			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	

Nausea subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Hypoaesthesia oral subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Paraesthesia oral subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	
Vomiting subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Skin and subcutaneous tissue disorders			
Pruritus subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 13 (7.69%) 2	
Onycholysis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Alopecia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	
Rash subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	1 / 13 (7.69%) 1	
Skin discolouration subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	
Renal and urinary disorders			
Micturition urgency subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 13 (7.69%) 1	
Pollakiuria subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Renal failure			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Renal failure chronic subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Urge incontinence subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	
Urinary incontinence subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 13 (7.69%) 1	
Back pain subjects affected / exposed occurrences (all)	5 / 15 (33.33%) 5	1 / 13 (7.69%) 1	
Bursitis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 13 (7.69%) 1	
Fracture pain subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 13 (0.00%) 0	
Mobility decreased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 13 (0.00%) 0	
Muscle spasms subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2	1 / 13 (7.69%) 1	
Musculoskeletal pain			

subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Osteoarthritis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	1 / 15 (6.67%)	2 / 13 (15.38%)	
occurrences (all)	1	2	
Spinal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Trigger finger			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Cellulitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Bronchitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	

Folliculitis		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Influenza		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Gastroenteritis		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Nasopharyngitis		
subjects affected / exposed	3 / 15 (20.00%)	0 / 13 (0.00%)
occurrences (all)	4	0
Oral candidiasis		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Onychomycosis		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Paronychia		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Pneumonia		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Pulpitis dental		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Rhinitis		
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	0
Sialoadenitis		
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0
Tooth infection		
subjects affected / exposed	2 / 15 (13.33%)	0 / 13 (0.00%)
occurrences (all)	2	0

Tracheitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	2 / 15 (13.33%)	0 / 13 (0.00%)	
occurrences (all)	4	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Urosepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Gout			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Hypercholesterolaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Iron deficiency			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Vitamin B12 deficiency			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Vitamin D deficiency			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 November 2011	<p>The protocol is being amended to eliminate the lowest dose (10 mg b.i.d.) based on the results from study CAFQ056A2208. The analyses showed that the dose of 10 mg b.i.d. was nonefficacious and there was a trend for improvement at the dose of 25 mg b.i.d. and a statistically significant improvement at the 100 mg b.i.d. dose. This suggests that patients are unlikely to benefit at the 10 mg b.i.d. dose but may start to see improvement at 25 mg b.i.d. As a result, the 10 mg b.i.d. dose (capsule strength 5 mg) will no longer be provided in this study.</p> <p>The amended protocol also eliminates the previous restrictions on the use of centrally acting anti-cholinergic medication. This exclusion was included in the original protocol as a general precaution to avoid unwarranted side effects due to (centrally mediated) anti-cholinergic effects in this patient population. Elimination of this restriction is in the patients' best interest as it provides investigators with additional treatment options where appropriate.</p> <p>A potential interaction between the study drug and isoflurane (an inhalational drug used for anesthesia in surgery) was found in a single animal experiment with mice, but was not seen in a bigger mouse study or in several other studies in rats. No experience in humans exists. Therefore, isoflurane is being added to the list of prohibited medications as a precautionary measure. This warning is already included in the Investigator Brochure, Patient Information Card, and the patient Informed Consent Form.</p>

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 study was terminated based on the results of studies CAFQ056A2222 and CAFQ056A2223 (due to lack of efficacy) and the sponsor's decision to terminate the program.

Notes: