

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

EudraCT number	2010-019418-25		
Trial protocol	IT FR DE FI		
Global end of trial date	15 October 2013		
Result version number	v1 (current)		
This version publication date	13 July 2016		
First version publication date	03 August 2015		
Community and an dis	CAE005CA3347		
Sponsor protocol code	CAFQ056A2217		
ISRCTN number	_		
ClinicalTrials.gov id (NCT number)	NCT01173731		
WHO universal trial number (UTN)			
Notes:	<u> </u>		
Notes.			
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:			
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:			

EU-CTR publication date: 13 July 2016

Notes:

Final
15 October 2013
No
1
Yes
15 October 2013
Yes

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.

ci iai:	
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:

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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:

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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

EU-CTR publication date: 13 July 2016

Recruitment details: -	
Screening details: The study population consisted of male of	or female patients with PD-LID who have completed selected
double-blind studies with AFQ056 or place	
Period 1 title	Open-label Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded
Are arms mutually exclusive?	Yes
·	AFQ056 10 mg b.i.d.
Arm description:	I .
The investigational drug, AFQ056, was p	rovided 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:	
morning and evening doses were taken a study drug for any reason, the patient w scheduled dose. Study drug was adminis	of capsules in the morning and in the evening as indicated. The at approximately 12-hour intervals. If a patient missed a dose of as instructed to not make up the missed dose with the next stered with a glass of water. Patients were instructed to not le. Patients were asked to avoid drinking grapefruit juice during
	AFQ056 25 mg b.i.d
Arm description:	
The investigational drug, AFQ056, was p	rovided 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:	
morning and evening doses were taken a study drug for any reason, the patient w scheduled dose. Study drug was adminis	of capsules in the morning and in the evening as indicated. The at approximately 12-hour intervals. If a patient missed a dose of as instructed to not make up the missed dose with the next stered with a glass of water. Patients were instructed to not le. Patients were asked to avoid drinking grapefruit juice during
	AFQ056 50 mg b.i.d.
Arm description:	
The investigational drug, AFQ056, was p	rovided as hard gelatin capsules.
Arm type	Experimental

EU-CTR publication date: 13 July 2016

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.

the study.			
	AFQ056 75 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.

	AFQ056 100 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.

	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	-

	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	-	-

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.

	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	±	±	
Gender categorical			
Units: Subjects			
Female			
Male			

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Reporting group title	AFQ056 10 mg b.i.d.
Reporting group description:	
	was provided as hard gelatin capsules.
Reporting group title	AFQ056 25 mg b.i.d
Reporting group description:	
<u> </u>	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 open-label study.	received at least one dose of open-label study medication during thi
Subject analysis set title	Safety Set (SS)
Subject analysis set type	Safety analysis
	•
Subject analysis set description:	
The SS consisted of all patients wh	ho received at least one dose of open-label study medication during d at least one post-baseline safety assessment.
The SS consisted of all patients wh	
The SS consisted of all patients whether the study and who had	d at least one post-baseline safety assessment. Changes from baseline in cognitive function as measured by
The SS consisted of all patients whethis open-label study and who had study and who had study and point title End point description: The study was terminated based of	d at least one post-baseline safety assessment. Changes from baseline in cognitive function as measured by
The SS consisted of all patients whethis open-label study and who had been point title End point description: The study was terminated based of to lack of efficacy) and the sponso	Changes from baseline in cognitive function as measured by the Mini-Mental State Examination (MMSE) total score ^[1] on the results of studies CAFQ056A2222 and CAFQ056A2223 (due
The SS consisted of all patients whethis open-label study and who had this open-label study and who had the sponso to lack of efficacy) and the sponso the sponso that the sponso the sponso that the sponso t	Changes from baseline in cognitive function as measured by the Mini-Mental State Examination (MMSE) total score ^[1] on the results of studies CAFQ056A2222 and CAFQ056A2223 (due or's decision to terminate the program.
The SS consisted of all patients whethis open-label study and who had study and who had study and point title End point description: The study was terminated based of	Changes from baseline in cognitive function as measured by the Mini-Mental State Examination (MMSE) total score ^[1] on the results of studies CAFQ056A2222 and CAFQ056A2223 (due or's decision to terminate the program.

least one statistical analysis for each primary end point.

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

	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

No statistical analyses for this end point

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
Dictionary name	MedDRA
Dictionary version	16.1
Reporting group title	AFQ056 10mg
Reporting group description:	
AFQ056 10mg	
Reporting group title	AFQ056 25mg
Reporting group description:	
AFQ056 25mg	
Reporting group title	AFQ056 100mg
Reporting group description:	
AFQ056 100mg	
Reporting group title	AFQ056 75mg
Reporting group description:	
AFQ056 75mg	
Reporting group title	AFQ056 50mg
Reporting group description:	
AFQ056 50mg	

	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
	I	[·
Respiratory arrest subjects affected / exposed	0 / 2 / 0 000/)	0 / 16 /0 000/)	0 / 10 /0 000/)
occurrences causally related to	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
treatment / all			
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			ĺ
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			ĺ
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]	İ
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	I		
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		[İ
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			ĺ
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			

Gastrooesophageal 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	I	1	
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	I	I	
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

	1	Ι	1
	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	
ychiatric 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	
vestigations			
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			

0 / 15 (0.00%)	2 / 13 (15.38%)	
0 / 0	0 / 2	
0 / 0	0 / 0	
1 / 15 (6.67%)	0 / 13 (0.00%)	
0 / 1	0 / 0	
0 / 0	0 / 0	
0 / 15 (0.00%)	0 / 13 (0.00%)	
0 / 0	0 / 0	
0 / 0	0 / 0	
0 / 15 (0.00%)	0 / 13 (0.00%)	
0 / 0	0 / 0	
0 / 0	0 / 0	
0 / 15 (0.00%)	1 / 13 (7.69%)	
0 / 0	0 / 1	
0 / 0	0 / 0	
1 / 15 (6.67%)	0 / 13 (0.00%)	
0 / 1	0 / 0	
0 / 0	0 / 0	
1 / 15 (6.67%)	0 / 13 (0.00%)	
0 / 1	0 / 0	
0 / 0	0 / 0	
	ĺ	
1 / 15 (6.67%)	0 / 13 (0.00%)	
0 / 1	0 / 0	
0 / 0	0 / 0	
	0 / 0 0 / 0 1 / 15 (6.67%) 0 / 1 0 / 0 0 / 15 (0.00%) 0 / 0 0 / 0 0 / 0 0 / 0 0 / 0 1 / 15 (6.67%) 0 / 1 0 / 0 1 / 15 (6.67%) 0 / 1 0 / 0 1 / 15 (6.67%) 0 / 1	0/0 0/2 0/0 0/0 1/15 (6.67%) 0/13 (0.00%) 0/1 0/0 0/0 0/0 0/15 (0.00%) 0/13 (0.00%) 0/0 0/0 0/15 (0.00%) 0/13 (0.00%) 0/0 0/0 0/15 (0.00%) 0/13 (0.00%) 0/0 0/1 0/0 0/1 0/0 0/1 0/0 0/0 1/15 (6.67%) 0/13 (0.00%) 0/1 0/0 1/15 (6.67%) 0/13 (0.00%) 0/1 0/0 1/15 (6.67%) 0/13 (0.00%) 0/1 0/0

l subjects official / summed	1 1		1
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	ĺ		Ĺ
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			İ
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			İ
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			j
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 /0 000/)	1 / 12 /7 (00/)	
occurrences causally related to treatment / all	0 / 15 (0.00%) 0 / 0	1 / 13 (7.69%) 0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
	1 7,7	, , , , , , , , , , , , , , , , , , ,	I
Infections and infestations	l l	ı I	l

rthritis 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	
leningitis			
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	
neumococcal 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	
neumonia			
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	
yelonephritis			
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	
eptic 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	
rinary 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 %

	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
		Ĭ	
Feeling hot subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1 (5.20 %)
			<u> </u>
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	I		
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Ejaculation disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Allergic cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	2 / 19 (10.53%)
occurrences (all)			
occurrences (an)	0	1	2
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Hyperventilation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	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			
	i	1	I
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)

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 (0 (0 00)	0 / 16 / 0 000/)	1 (10 (5 050()
	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	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Incisional hernia subjects affected / exposed occurrences (all)	0 / 3 (0.00%)	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Tendon rupture subjects affected / exposed occurrences (all)	0 / 3 (0.00%)	0 / 16 (0.00%) 0	0 / 19 (0.00%)
Wound			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Arrhythmia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Atrial fibrillation			
subjects affected / exposed		0 / 1□	0 / 19 (0.00%)

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 occurrences (all)	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
Dualinasia			<u>-</u>
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)	О	4	2
Speech disorder			

subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Stupor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
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Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Bicytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 16 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
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Eosinophilia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Eye disorders			
Altered visual depth perception			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
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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	1 / 3 (33.33%)	2 / 16 (12.50%)	1 / 19 (5.26%)
occurrences (all)	1	2	1
Hypoaesthesia oral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Paraesthesia oral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	0 / 16 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Onycholysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Skin discolouration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	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)			
occurrences (an)	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
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Endocrine disorders Hyperthyroidism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
occurrences (un)	U	U	U
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 / 2 /0 000/)	0 / 16 /0 000/)	2 / 10 /10 F20/ \
occurrences (all)	0 / 3 (0.00%)	0 / 16 (0.00%)	2 / 19 (10.53%)
occurrences (aii)	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
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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 / 2 / 0 000/)	1 / 16 /6 250/	0 / 10 / 0 000/)
occurrences (all)	0 / 3 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (un)	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
	l		

Folliculitis subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0 / 3 (0.00%)	0 / 10 (0.00 %)	1 19 (3.20%)
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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	
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
Phinitic			
Rhinitis subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)			
occurrences (un)	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%)
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Tracheitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Uning my tract infection			
Urinary tract infection subjects affected / exposed	0 / 3 (0.00%)	1 / 16 (6.25%)	3 / 19 (15.79%)
occurrences (all)			
occurrences (un)	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
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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
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	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	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Ejaculation disorder			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Allergic cough			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	

Abnormal dreams subjects affected / exposed	2 / 45 / 43 - 55 - 5		
	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			
	1 0 / 4 5 / 0 000/ \ \	1 / 12 /7 600/)	
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	

Impulsive behaviour			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Illusion			
subjects affected / exposed	2 / 15 (13.33%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Insomnia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Jealous delusion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
		U	
Nightmare			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Libido increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Panic attack			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	_		
occurrences (air)	0	0	
Pathological gambling			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Investigations			
Amylase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Blood creatine phosphokinase			
increased			
subjects affected / exposed	2 / 15 (13.33%)	0 / 13 (0.00%)	
occurrences (all)	2	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)	О	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	0 / 15 /0 000/)	0 / 12 / 0 000/)	
occurrences (all)	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (an)	0	0	
Neutrophil count increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Platelet count decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Red blood cell count decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
decan enece (an)			
Weight decreased			
subjects affected / exposed	1 / 15 (6.67%)	2 / 13 (15.38%)	
occurrences (all)	1	2	
White blood cell count decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Weight increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
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White blood cells urine positive			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural			
complications			
Contusion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Fall			
subjects affected / exposed	1 / 15 (6.67%)	3 / 13 (23.08%)	
occurrences (all)			
occurrences (un)	1	7	
Fracture			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Laceration			

1	1	Ī	1
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 /0 000/ >	0 / 12 / 0 000/ >	
	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Cognitive disorder			
subjects affected / exposed	0 / 15 /0 000/ \	0 / 12 /0 000/ \	
	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Carpal tunnel syndrome			
Carpar turner syndrome	l		ı

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 / 13 (0.00%)	1 / 13 (7.0970)
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Disturbance in attention	_ , , _ , , , , ,	
subjects affected / exposed occurrences (all)	2 / 15 (13.33%)	0 / 13 (0.00%)
occurrences (an)	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		
турствонна	I	

subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Hypoaesthesia subjects affected / exposed	1 / 15 /6 670/\	0 / 13 (0 00%)	
occurrences (all)	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 / 0 000/)	1 / 12 /7 (00/)	
occurrences (all)	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	
	I		

subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Stupor			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
		_	
Syncope subjects affected / exposed	0 (45 (0 000()	0 (42 (0 000)	
occurrences (all)	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (an)	0	0	
Blood and lymphatic system disorders			
Bicytopenia subjects affected / exposed	1 / 15 / 6 670/)	0 / 12 / 0 000/)	
occurrences (all)	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (an)	1	0	
Anaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Leukopenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Eosinophilia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Ear and labyrinth disorders Tinnitus			
subjects affected / exposed	2 / 15 (13.33%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Vortigo			
Vertigo subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
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Eye disorders			
Altered visual depth perception subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0 0 13 (0.00 %)	1	
	Ŭ	<u> </u>	
Cataract			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Diplopia			

subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Photophobis			
Photophobia subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0 / 13 (0.00%)	0 / 13 (0.00%)	
(411)		J	
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	
		Ĭ	
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	
		Ĭ	
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			
Dry mouth subjects affected / exposed	2 / 15 (13.33%)	0 / 13 (0.00%)	
occurrences (all)	2 / 13 (13.33%)	0 / 13 (0.00%)	
Coodin Gricos (dir)		ľ	
Gastrointestinal hypermotility			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
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Nausea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Hypoaesthesia oral			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Paraesthesia oral			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Onycholysis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Alopecia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 15 (6.67%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Skin discolouration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Renal failure			

subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Renal failure chronic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Urge incontinence			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Uningsus in continuo			
Urinary incontinence subjects affected / exposed	0 / 15 (0 000/)	0 / 12 /0 000/)	
	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue			
disorders Arthralgia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1 13 (7.03 70)	
,	Ŭ	1	
Back pain			
subjects affected / exposed	5 / 15 (33.33%)	1 / 13 (7.69%)	
occurrences (all)	5	1	
Bursitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
For the second			
Fracture pain subjects affected / exposed	1 / 15 / 6 670/	0 / 12 / 0 000/)	
	1 / 15 (6.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Mobility decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	2 / 15 (13.33%)	1 / 13 (7.69%)	
occurrences (all)	2 / 13 (13.33 70)	1 / 13 (7.09%)	
(4)		1	
Musculoskeletal pain			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%)	1 / 13 (7.69%) 1	
Musculoskeletal stiffness subjects affected / exposed occurrences (all)	1 / 15 (6.67%)	0 / 13 (0.00%) 0	

Folliculitis	1		
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	

Were there any global substantial amendments to the protocol? Yes

09 November 2011

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.

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.

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.

Notes:

Were there any global interruptions to the trial? No

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: