Clinical trial results:
A double blind, randomized, placebo-controlled study to evaluate safety, tolerability, efficacy and preliminary dose-response of BAF312 in patients with active dermatomyositis

Summary

EudraCT number	2013-001799-39
Trial protocol	HU CZ PL BE
Global end of trial date	17 February 2016

Results information

Result version number	v1 (current)
This version publication date	01 December 2016
First version publication date	01 December 2016

Trial information

Trial identification

Sponsor protocol code	CBAF312X2206

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02029274
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	17 February 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 February 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of different doses of BAF312 after 6 months of treatment in active DM patients as assessed by manual muscle testing using the MMT-24 scoring system

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	15 November 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 4
Country: Number of subjects enrolled	Japan: 3
Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	17
EEA total number of subjects	4

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	17
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was composed of 2 periods: a double-blind period 1 with BAF312 administered at different daily doses (0.5, 2, 10 mg and placebo) and a fixed-dose Period 2 in which BAF312 was administered to all randomized at the dose of 2 mg daily .

Pre-assignment

Screening details:

Participants were randomized to each treatment group in a1:1:1:1 ratio.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	BAF312 0.5mg

Arm description:

During period 1, participants were uptitrated daily from BAF312 0.25 mg to 0.5 mg over a 10 day period. After, participants continued on 0.5 mg daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Siponimod
Investigational medicinal product code	BAF312
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

During period 1, participants were uptitrated daily from BAF312 0.25 mg to 0.5 mg over a 10 day period. After, participants continued on 0.5 mg daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.

Arm title	BAF312 2mg

Arm description:

During period 1, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Siponimod
Investigational medicinal product code	BAF312
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

During period 1, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.

Arm title	BAF312 10 mg

Arm description:

During period 1, participants were uptitrated daily from BAF312 0.25 mg to 10.0 mg over a 10 day period. After, participants continued on 10.0 mg daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Siponimod
Investigational medicinal product code	BAF312
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

During period 1, participants were uptitrated daily from BAF312 0.25 mg to 10.0 mg over a 10 day period. After, participants continued on 10.0 mg daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.

Arm title	Placebo

Arm description:

During period 1, participants received matching placebo daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

During period 1, participants received matching placebo daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.

Number of subjects in period 1	BAF312 0.5mg	BAF312 2mg	BAF312 10 mg
Started	5	4	4
Completed	4	4	2
Not completed	1	0	2
Adverse event, non-fatal	1	-	2

Number of subjects in period 1	Placebo
Started	4
Completed	2
Not completed	2
Adverse event, non-fatal	2

Baseline characteristics

Reporting groups	
Reporting group title	BAF312 0.5mg
Reporting group description:	
During period 1, participants were uptitrated daily from BAF312 0.25 mg to 0.5 mg over a 10 day period. After, participants continued on 0.5 mg daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.	
Reporting group title	BAF312 2mg
Reporting group description:	
During period 1, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.	
Reporting group title	BAF312 10 mg
Reporting group description:	
During period 1, participants were uptitrated daily from BAF312 0.25 mg to 10.0 mg over a 10 day period. After, participants continued on 10.0 mg daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.	
Reporting group title	Placebo
Reporting group description:	
During period 1, participants received matching placebo daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.	

Reporting group values	BAF312 0.5mg	BAF312 2mg	BAF312 10 mg
Number of subjects	5	4	4
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5	4	4
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	51.8	44	51.8
standard deviation	± 16.72	± 6.98	± 4.79
Gender, Male/Female Units: Subjects			
Female	4	2	4
Male	1	2	0

Reporting group values	Placebo	Total	
Number of subjects	4	17	

Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	17	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	48		
standard deviation	± 10.61	-	
Gender, Male/Female Units: Subjects			
Female	3	13	
Male	1	4	

End points

End points reporting groups

Reporting group title	BAF312 0.5mg
Reporting group description:	
During period 1, participants were uptitrated daily from BAF312 0.25 mg to 0.5 mg over a 10 day period. After, participants continued on 0.5 mg daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.	
Reporting group title	BAF312 2mg
Reporting group description:	
During period 1, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.	
Reporting group title	BAF312 10 mg
Reporting group description:	
During period 1, participants were uptitrated daily from BAF312 0.25 mg to 10.0 mg over a 10 day period. After, participants continued on 10.0 mg daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.	
Reporting group title	Placebo
Reporting group description:	
During period 1, participants received matching placebo daily for up to 24 weeks. During period 2, participants were uptitrated daily from BAF312 0.25 mg to 2.0 mg over a 10 day period. After, participants continued on 2.0 mg daily for up to 24 weeks.	

Primary: Change from baseline in Manual Muscle Testing - 24 muscles (MMT-24) score

End point title	Change from baseline in Manual Muscle Testing - 24 muscles (MMT-24) score
End point description:	
Each muscles tested was evaluated on a 0 - 10 scale where 0 indicated the weakest muscle score and 10 indicated the strongest muscle score. The total MMT24 score ranged from 0 - 240, where an increasing trend in the values indicates improvement. A positive change from baseline indicates improvement.	
End point type	Primary
End point timeframe:	
6 months	

End point values	BAF312 0.5mg	BAF312 2mg	BAF312 10 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	3
Units: score on a scale				
least squares mean (standard error)	28.286 (± 8.1539)	12.367 (± 7.0967)	14.026 (± 8.1541)	27.735 (± 8.2175)

Statistical analyses

Statistical analysis title	Change from baseline in MMT-24 score
Comparison groups	Placebo v BAF312 0.5mg
Number of subjects included in analysis	6
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9621
Method	Repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	0.551
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.447
upper limit	23.549
Variability estimate	Standard error of the mean
Dispersion value	11.5519

Statistical analysis title	Change from baseline in MMT-24 score
Comparison groups	BAF312 2mg v Placebo
Number of subjects included in analysis	7
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1637
Method	Repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-15.368
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.128
upper limit	6.391
Variability estimate	Standard error of the mean
Dispersion value	10.9297

Statistical analysis title	Change from baseline in MMT-24 score
Comparison groups	Placebo v BAF312 10 mg
Number of subjects included in analysis	6
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2409
Method	Repeated measures
Parameter estimate	Mean difference (net)
Point estimate	-13.709

Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.806
upper limit	9.388
Variability estimate	Standard error of the mean
Dispersion value	11.6016

Secondary: BAF312 plasma concentration

End point title	BAF312 plasma concentration

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	BAF312 0.5mg	BAF312 2mg	BAF312 10 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[1]	0[2]	0[3]	0[4]
Units: ng/mL				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[1] - Study was terminated prematurely due to futility. Primary outcome disclosed only.

[2] - Study was terminated prematurely due to futility. Primary outcome disclosed only.

[3] - Study was terminated prematurely due to futility. Primary outcome disclosed only.

[4] - Study was terminated prematurely due to futility. Primary outcome disclosed only.

Statistical analyses

No statistical analyses for this end point

Secondary: Peripheral blood lymphocyte counts

End point title	Peripheral blood lymphocyte counts

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	BAF312 0.5mg	BAF312 2mg	BAF312 10 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[5]	0[6]	0[7]	0[8]
Units: Percent				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[5] - Study was terminated prematurely due to futility. Primary outcome disclosed only.

[6] - Study was terminated prematurely due to futility. Primary outcome disclosed only.

[7] - Study was terminated prematurely due to futility. Primary outcome disclosed only.

[8] - Study was terminated prematurely due to futility. Primary outcome disclosed only.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Manual Muscle Testing - 24 muscles (MMT-24) score

End point title	Change from baseline in Manual Muscle Testing - 24 muscles (MMT-24) score

End point description:

End point type	Secondary

End point timeframe:

3 months

End point values	BAF312 0.5mg	BAF312 2mg	BAF312 10 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[9]	0[10]	0[11]	0[12]
Units: score on a scale				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[9] - The study was prematurely terminated based on the results of an interim analysis.

[10] - The study was prematurely terminated based on the results of an interim analysis.

[11] - The study was prematurely terminated based on the results of an interim analysis.

[12] - The study was prematurely terminated based on the results of an interim analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: 6 Minutes Walking Distance (6-MWD) test

End point title	6 Minutes Walking Distance (6-MWD) test

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	BAF312 0.5mg	BAF312 2mg	BAF312 10 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[13]	0[14]	0[15]	0[16]
Units: meters				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[13] - The study was prematurely terminated based on the results of an interim analysis.

[14] - The study was prematurely terminated based on the results of an interim analysis.

[15] - The study was prematurely terminated based on the results of an interim analysis.

[16] - The study was prematurely terminated based on the results of an interim analysis.

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 reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Period 1 Placebo
Reporting group description:	
Period 1 Placebo	
Reporting group title	Period 1 BAF312 0.5 mg/day
Reporting group description:	
Period 1 BAF312 0.5 mg/day	
Reporting group title	Period 1 BAF312 2 mg/day
Reporting group description:	
Period 1 BAF312 2 mg/day	
Reporting group title	Period 1 BAF312 10 mg/day
Reporting group description:	
Period 1 BAF312 10 mg/day	
Reporting group title	Period 2 Placebo /BAF312 2 mg/day
Reporting group description:	
Period 2 Placebo /BAF312 2 mg/day	
Reporting group title	Period 2 BAF312 0.5 mg/day/BAF312 2 mg/day
Reporting group description:	
Period 2 BAF312 0.5 mg/day/BAF312 2 mg/day	
Reporting group title	Period 2 BAF312 2 mg/day/BAF312 2 mg/day
Reporting group description:	
Period 2 BAF312 2 mg/day/BAF312 2 mg/day	
Reporting group title	Period 2 BAF312 10 mg/day/BAF312 2 mg/day
Reporting group description:	
Period 2 BAF312 10 mg/day/BAF312 2 mg/day	

Serious adverse events	Period 1 Placebo	Period 1 BAF312 0.5 mg/day	Period 1 BAF312 2 mg/day
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Laceration			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (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
Procedural pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (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
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (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
Syncope			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (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
Skin and subcutaneous tissue disorders			
Dermatomyositis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 4 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 4 (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

Serious adverse events	Period 1 BAF312 10 mg/day	Period 2 Placebo /BAF312 2 mg/day	Period 2 BAF312 0.5 mg/day/BAF312 2 mg/day
Total subjects affected by serious			

adverse events			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
Procedural pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatomyositis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (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			
Pneumonia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (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

Serious adverse events	Period 2 BAF312 2 mg/day/BAF312 2 mg/day	Period 2 BAF312 10 mg/day/BAF312 2 mg/day	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (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			
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatomyositis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (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	Period 1 Placebo	Period 1 BAF312 0.5 mg/day	Period 1 BAF312 2 mg/day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	1 / 4 (25.00%)	4 / 4 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroadenoma of breast			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Internal limiting membrane peeling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Non-cardiac chest pain			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Allergic sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Confusional state			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
Carbon monoxide diffusing capacity decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Pulmonary function test abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Post procedural inflammation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness postural			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Exertional headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Migraine			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Transient global amnesia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Blepharospasm			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chorioretinal atrophy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Eye swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Eyelid oedema			

subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Retinal vein occlusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Vitreous detachment			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Gingival recession			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Generalised erythema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Skin fissures			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	2
Musculoskeletal chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Osteonecrosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cellulitis orbital			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Dacryocystitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Herpes simplex			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	3 / 4 (75.00%)
occurrences (all)	0	0	6
Oral candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1

Non-serious adverse events	Period 1 BAF312 10 mg/day	Period 2 Placebo /BAF312 2 mg/day	Period 2 BAF312 0.5 mg/day/BAF312 2 mg/day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	2 / 5 (40.00%)	1 / 4 (25.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroadenoma of breast			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
Internal limiting membrane peeling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Fatigue			
subjects affected / exposed	2 / 4 (50.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Allergic sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pulmonary congestion			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
Carbon monoxide diffusing capacity decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary function test abnormal			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Post procedural inflammation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness postural			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Exertional headache			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 4 (50.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Migraine			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Transient global amnesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Blepharospasm			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Chorioretinal atrophy			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Conjunctival haemorrhage			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eyelid oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Retinal vein occlusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vitreous detachment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gingival recession			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Ecchymosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Generalised erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			

subjects affected / exposed	2 / 4 (50.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Osteonecrosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cellulitis orbital			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dacryocystitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Influenza			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Period 2 BAF312 2 mg/day/BAF312 2 mg/day	Period 2 BAF312 10 mg/day/BAF312 2 mg/day	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	2 / 4 (50.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroadenoma of breast			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Surgical and medical procedures			
Internal limiting membrane peeling			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Oedema peripheral			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Allergic sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Nasal congestion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Productive cough			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Pulmonary congestion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Pulmonary hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Investigations			
Carbon monoxide diffusing capacity decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Pulmonary function test abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Post procedural inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness postural			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Exertional headache			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	2 / 4 (50.00%)	1 / 4 (25.00%)	
occurrences (all)	2	1	
Migraine			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Syncope			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Transient global amnesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Blepharospasm			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Chorioretinal atrophy			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Conjunctival haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Eye swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Eyelid oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Retinal vein occlusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Vitreous detachment			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Vitreous floaters			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Gingival recession			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	

Nausea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Ecchymosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	2	
Eczema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Generalised erythema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Pruritus generalised			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Skin fissures			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Osteonecrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Cellulitis orbital			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Dacryocystitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Herpes simplex			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Herpes zoster			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Oral candidiasis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Skin infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2013	The reason for amending the protocol was the expansion of the study to other countries (Japan) where the MCT system was not approved yet. The cardiac monitoring was performed with a Holter ECG instead of the device planned in the initial sites. The technical properties of the Holter device require 4 additional visits to be added to the schedule, in order to apply the Holter device. Furthermore, typos were corrected and clarifications added.
15 April 2014	The reason for amending the protocol was the addition of recent findings in a mouse carcinogenicity study. The additions made to the protocol reflected the changes made in the Investigator's Brochure version 11 and the patients' ICF. A section of efficacy data in PM/DM was updated with final data of a completed PoC trial that had become available. The upper age limit was increased from 65 years to 70 years based on recent investigator feedback, to better accommodate the patient population in need for new therapy. Based on the large safety database with more than 1500 patients exposed to BAF312 in 15 completed and 8 ongoing trials (as of 5 March 2014), the risk-benefit profile of BAF312 was considered suitable for patients up to the age of 70. The study stopping rules were modified to allow for a full safety review prior to discontinuation of all patients in case of 2 patients experiencing a study drug related adverse event, as specified in the stopping rules. Considering the relatively long treatment duration of 48 weeks and 56 patients to be enrolled, chances were high to observe SAEs that could be judged as related because a relation could never be completely excluded. In such a situation it could be unethical to discontinue treatment immediately in all patients; in particular in those who were benefiting, at least until a full safety review had been conducted.
01 July 2015	The purpose of this amendment was to update the eligibility criteria, to adapt the protocol to newly available information, and to include a broader population that better reflects the patient population in need of new therapeutic options. Furthermore, typing errors were corrected, and clarifications were added.
27 July 2015	The purpose of this amendment was to update the contact data for the Translational Medicine Expert, and to correct inconsistencies between synopsis and protocol body. Furthermore, Figure 3-1 was updated regarding time windows.

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 prematurely after an interim analysis for futility. The study did not provide any evidence for efficacy of BAF312 in dermatomyositis. There were no safety concerns.

Notes: