Clinical trial results:
Clinical study to investigate safety, tolerability, efficacy, pharmacokinetics and pharmacodynamics of multiple doses of the human GATA-3-specific DNAzyme solution SB010 in patients with mild allergic asthma – A randomised, double-blind, parallel, multicentre, phase-IIa study –

Summary

EudraCT number	2012-003570-77
Trial protocol	DE
Global end of trial date	27 November 2013

Results information

Result version number	v1
This version publication date	05 November 2021
First version publication date	05 November 2021

Trial information

Trial identification

Sponsor protocol code	SB010/04/2012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01743768
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sterna biologicals GmbH & Co KG
Sponsor organisation address	Bismarckstraße 7, Marburg, Germany, 35037
Public contact	Clinical Trial Manager, Sterna biologicals GmbH & Co. KG , clinicaltrials@sterna-biologicals.com
Scientific contact	Clinical Trial Manager, Sterna biologicals GmbH & Co. KG , clinicaltrials@sterna-biologicals.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 August 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the influence of multiple doses of inhaled SB010 on the late phase response (4 – 7 hours) after allergen challenge (AC).

The rationale of the study was to investigate the efficacy, pharmacokinetics, and pharmacodynamics of multiple doses of inhaled SB010 in patients with documented mild allergic asthma. This was done by analysing the late asthmatic response (LAR), following allergen challenge (AC) after a 4-week treatment period. The study consisted of 2 parallel treatment groups and was randomised and placebo-controlled. For an individual patient, the total duration of study participation was estimated at most 149 days.

The investigational medicinal product (IMP) SB010 contains the DNAzyme hgd40 (new class of antisense oligonucleotide therapeutics), which targets the mRNA of the transcription factor GATA-3. GATA-3 is the key regulatory factor of T helper cells 2 (Th2)-driven immune responses. Development of asthma is often correlated with a malfunction of immune system.

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles that have their origin in the currently valid Declaration of Helsinki, and are consistent with ICH-GCP (January 1997) and applicable regulatory requirements.

All laboratory tests and procedures used during the study are well established and validated. Adverse events were monitored from the time of signing the informed consent to the end of the study (or study discontinuation).

Background therapy: -

Evidence for comparator:

Abbreviations used in this entry

AC=allergen challenge
AUC(4-7) FEV1=Area under the FEV1 curve from 4 h to 7 h
AUC(0-12)=The area under the plasma concentration-time curve from zero to 12 h
Cmax=Concentration maximum, highest observed plasma concentration of the measured concentration-time profile
FEV1=Forced expiratory volume in 1 second
FVC=Forced vital capacity
h=hour
hgd40=Active principle of the IMP SB010, a human GATA-3-specific DNAzyme
IMP=Investigational medicinal product
LAR=Late asthmatic response
OD=Once daily
t½=Half-life; Time it takes for the concentration of a substance in the body to be reduced by one half
tmax=Time of maximum concentration

Actual start date of recruitment	11 December 2012
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	Germany: 43
Worldwide total number of subjects	43
EEA total number of subjects	43

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)	43
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Overall, 43 adult white male subjects (18 to 60 years) with documented mild asthma (FEV1 value of FEV1 ≥ 70% of the predicted normal value) were eligible for enrolment into the trial and to randomisation.

Pre-assignment

Screening details:

Asthma patients were screened according to inclusion and exclusion criteria. Written informed consent was obtained prior to participation in the study. Only patients with a documented or known biphasic reaction to allergen challenge (AC) -- early-phase and late-phase response -- were enrolled; bronchoprovocation at screening was with methacholine.

Period 1

Period 1 title	Overall treatment (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

Blinding implementation details:

Double-blind design. To ensure double-blinding, the study medications (SB010 and placebo) were identical with respect of their outer appearance, odour, packaging, and labelling.

Arms

Are arms mutually exclusive?	Yes
Arm title	SB010

Arm description:

Patients received SB010.

Each patient was treated for 28 days once daily (OD) with the test product (10 mg hgd40 in 2 mL solution concentration: 5 mg/mL).

Arm type	Experimental
Investigational medicinal product name	SB010
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

10 mg hgd40 in 2 mL solution (concentration: 5.0 mg/mL), oral inhalation (nebuliser)

SB010 (10 mg hgd40 in 2 mL solution as oral inhalation solution (nebuliser) was administered in a dosing interval of 24 h for 28 consecutive days (Day 1 to Day 28) using a controlled inhalation system (AKITA2 APIXNEB®). Inhalations were to be performed in the morning at the same time of the day.

On Day 1 (Visit 6, initial IMP), Day 6 ± 1 (Visit 7), Day 13 ± 1 (Visit 8), Day 20 ± 1 (Visit 9), Day 26 ± 1 (Visit 10) and Day 28 (Visit 11, therapy end) trained study personnel supervised the filling of the AKITA2 APIXNEB® nebuliser and the inhalation of the IMP solution by the patient. On the other treatment days patients self-administered the IMP solution once daily via AKITA2 APIXNEB® inhalation device.

Arm title	Placebo

Arm description:

Patients received Placebo.

Each patient received for 28 days once daily (OD) placebo (2 mL phosphate-buffered saline solution).

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

Placebo in 2 mL solution, oral inhalation (nebuliser)

Placebo treatment (2 mL placebo nebuliser solution (phosphate-buffered saline) was administered in a dosing interval of 24 h for 28 consecutive days (Day 1 to Day 28) using a controlled inhalation system (AKITA2 APIXNEB®). Inhalations were performed in the morning at the same time of the day.

On Day 1 (Visit 6, initial IMP), Day 6 ± 1 (Visit 7), Day 13 ± 1 (Visit 8), Day 20 ± 1 (Visit 9), Day 26 ± 1 (Visit 10) and Day 28 (Visit 11, therapy end) trained study personnel supervised the filling of the AKITA2 APIXNEB® nebuliser and the inhalation of the IMP solution by the patient. On the other treatment days patients self-administered the IMP solution once daily via AKITA2 APIXNEB® inhalation device.

Number of subjects in period 1	SB010	Placebo
Started	22	21
Completed	21	20
Not completed	1	1
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	SB010
Reporting group description:	
Patients received SB010. Each patient was treated for 28 days once daily (OD) with the test product (10 mg hgd40 in 2 mL solution concentration: 5 mg/mL).	
Reporting group title	Placebo
Reporting group description:	
Patients received Placebo. Each patient received for 28 days once daily (OD) placebo (2 mL phosphate-buffered saline solution).	

Reporting group values	SB010	Placebo	Total
Number of subjects	22	21	43
Age categorical Units: Subjects			
Adults (18-64 years)	22	21	43
Age continuous Units: years			
arithmetic mean	33.8	37.9	
standard deviation	± 9.4	± 12.1	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	22	21	43
Race Units: Subjects			
Caucasian	22	21	43

End points

End points reporting groups

Reporting group title	SB010

Reporting group description:

Patients received SB010.

Each patient was treated for 28 days once daily (OD) with the test product (10 mg hgd40 in 2 mL solution concentration: 5 mg/mL).

Reporting group title	Placebo

Reporting group description:

Patients received Placebo.

Each patient received for 28 days once daily (OD) placebo (2 mL phosphate-buffered saline solution).

Primary: 1_AUC for FEV1 in late phase response (4-7 h) after allergen challenge

End point title	1_AUC for FEV1 in late phase response (4-7 h) after allergen challenge

End point description:

Area under the curve (AUC) for FEV1, expressed as a percentage of the baseline FEV1 during late asthmatic response (4 to 7 h after allergen challenge), after administration of multiple doses of inhaled SB010.

Bronchial AC was performed with allergen extracts according to the allergens used for the skin prick test. For an individual patient, the allergen chosen was based on a positive skin prick test. A safe starting concentration for the inhaled aeroallergen was calculated using results of the skin prick dilution test performed at Visit 2 and the methacholine challenge performed at Visit 1.

Day -1 (enrolment i.e. before treatment)
Day 28 (treatment end)

End point type	Primary

End point timeframe:

After an allergen challenge (AC) at visit 4 (Day -1, enrolment) and at visit 11 (Day 28, end of the study).
Measurement time points for LAR were 4, 5, 6, and 7 hours after AC.

End point values	SB010	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[1]	18[2]		
Units: hour				
arithmetic mean (standard deviation)				
Day -1	0.664 (± 0.396)	0.592 (± 0.387)		
Day 28	0.440 (± 0.395)	0.600 (± 0.569)		

Notes:
[1] - Intention to treat population

[2] - Intention to treat population

Statistical analyses

Statistical analysis title	Analysis of covariance

Statistical analysis description:

Comparison of AUC4-7FEV1, at visit 11 between the treatment groups by analysis of covariance, with factors treatment and covariate AUC4-7FEV1 , at visit 4, respectively 2.

Comparison groups	SB010 v Placebo
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021
Method	ANCOVA
Parameter estimate	Mean difference of LS means
Confidence interval	
level	95 %

Secondary: 2_AUC for FEV1 in late phase response (4-7 h) after allergen challenge (Absolute change)

End point title	2_AUC for FEV1 in late phase response (4-7 h) after allergen challenge (Absolute change)

End point description:

AUC for FEV1 in late phase response (4-7 h) after allergen challenge (Absolute change)

For details please refer to endpoint #1.

The results are expressed as absolute change and are based on the results shown in endpoint #1. The results for absolute change reflect the effect of treatment on the lung function. Negative values imply improvement of lung function (i.e. less pronounced decline of lung function during the time interval from 4 to 7 hours after AC, considering the time of testing before and after treatment with SB010).

End point type	Secondary

End point timeframe:

After an allergen challenge (AC) at visit 4 (Day -1, enrolment) and at visit 11 (Day 28, end of the study).
Measurement time points for LAR were 4, 5, 6, and 7 hours after AC.

End point values	SB010	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[3]	18[4]		
Units: hour				
arithmetic mean (standard deviation)	-0.224 (± 0.277)	0.007 (± 0.308)		

Notes:

[3] - Intention to treat population

[4] - Intention to treat population

Statistical analyses

No statistical analyses for this end point

Secondary: 3_AUC for FEV1 in late phase response (4-7 h) after allergen challenge (Relative change)

End point title	3_AUC for FEV1 in late phase response (4-7 h) after allergen challenge (Relative change)

End point description:

AUC for FEV1 in late phase response (4-7 h) after allergen challenge (Relative change)

The results are expressed as percent change and are based on the results shown in endpoint #1.

The results for relative change reflect the effect of treatment on the lung function.

As shown in the Table below, a negative value implies an improvement of lung function (i.e. less pronounced decline of lung function during the time interval from 4 to 7 hours after AC, considering the time of testing before and after treatment with SB010).

End point type	Secondary

End point timeframe:

After an allergen challenge (AC) at visit 4 (Day -1, enrolment) and at visit 11 (Day 28, end of the study).
Measurement time points for LAR were 4, 5, 6, and 7 hours after allergen challenge (AC).

End point values	SB010	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[5]	18[6]		
Units: percent				
number (not applicable)	-33.7	1.4		

Notes:

[5] - Intention to treat population

A negative value implies an improvement in lung function.

[6] - Intention to treat population

A positive value implies a decline in lung function.

Statistical analyses

No statistical analyses for this end point

Secondary: 4_ Pharmacokinetic variables: maximum plasma concentration (Cmax)

End point title	4_ Pharmacokinetic variables: maximum plasma concentration

	(Cmax)[7]

End point description:

Pharmacokinetic variables: maximum plasma concentration (Cmax)

hgd40 plasma concentrations after first inhalation (Day 1) and last day of treatment i.e. after 28 days of treatment (Day 29).

hgd40 is the active principle of the IMP SB010.
hgd40 plasma concentrations was determined using a validated method (hybridisation ELISA) to capture the hgd40).

End point type	Secondary

End point timeframe:

First day of treatment (Day 1) and Day 28, of treatment: before treatment 0 min, and after treatment at 5, 10, 15, 20, 30, 45 min; 1, 1.5, 2, 4, 6, 8, 12, 24 h.

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Results for the SB010 arm were evaluated descriptively.

End point values	SB010			
Subject group type	Reporting group			
Number of subjects analysed	22[8]			
Units: Percent				
geometric mean (confidence interval 95%)				
Day 1	3.523 (2.229 to 5.566)			
Day 29	3.867 (2.483 to 6.020)			

Notes:

[8] - Safety analysis set

N=21 (Day 1)
N=22 (Day 29)

Statistical analyses

No statistical analyses for this end point

Secondary: 5_Pharmacokinetic variables: time to reach maximum plasma concentration (tmax)

End point title	5_Pharmacokinetic variables: time to reach maximum plasma concentration (tmax)[9]

End point description:

Time to reach maximum plasma concentration (tmax)

For further details please see endpoint #4.

End point type	Secondary

End point timeframe:

First day of treatment (Day 1) and Day 28 of treatment: before treatment 0 min, and after treatment at 5, 10, 15, 20, 30, 45 min; 1, 1.5, 2, 4, 6, 8, 12, 24 h.

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Results for the SB010 arm were evaluated descriptively.

End point values	SB010			
Subject group type	Reporting group			
Number of subjects analysed	22[10]			
Units: hour				
median (full range (min-max))				
Day 1	0.717 (0.33 to 1.00)			
Day 29	2.825 (0.90 to 63.98)			

Notes:

[10] - Safety analysis set

N=21 (Day 1)
N=22 (Day 29)

Statistical analyses

No statistical analyses for this end point

Secondary: 6_Pharmacokinetic variable: half-life (t½)

End point title	6_Pharmacokinetic variable: half-life (t½)[11]

End point description:

Half-life (t½).

For further details please see endpoint #4

End point type	Secondary

End point timeframe:

First day of treatment (Day 1) and Day 28 of treatment: before treatment 0 min, and after treatment at 5, 10, 15, 20, 30, 45 min; 1, 1.5, 2, 4, 6, 8, 12, 24 h.

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Results for the SB010 arm were evaluated descriptively.

End point values	SB010			
Subject group type	Reporting group			
Number of subjects analysed	16[12]			
Units: hour				
geometric mean (confidence interval 95%)				
Day 1	1.431 (1.176 to 1.742)			
Day 29	1.624 (1.314 to 2.008)			

Notes:

[12] - Safety analysis set

N=16 (Day 1)
N=15 (Day 29)

Statistical analyses

No statistical analyses for this end point

Secondary: 7_Pharmacokinetic variable: area under the plasma concentration-time curve from zero to 12 h [AUC(0-12)]

End point title	7_Pharmacokinetic variable: area under the plasma concentration-time curve from zero to 12 h [AUC(0-12)][13]

End point description:

Pharmacokinetic variable: area under the plasma concentration-time curve from zero to 12 h [AUC(0-12)].

For further details please see endpoint #4.

AUC(0-12)=The area under the plasma concentration-time curve from zero to 12 h

End point type	Secondary

End point timeframe:

First day of treatment (Day 1) and Day 28 of treatment: before treatment 0 min, and after treatment at 5, 10, 15, 20, 30, 45 min; 1, 1.5, 2, 4, 6, 8, 12, 24 h.

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Results for the SB010 arm were evaluated descriptively.

End point values	SB010			
Subject group type	Reporting group			
Number of subjects analysed	22[14]			
Units: ng.h/mL				
geometric mean (confidence interval 95%)				
Day 1	5.330 (2.851 to 9.965)			
Day 29	4.992 (2.502 to 9.961)			

Notes:

[14] - Safety analysis set

N=21 (Day 1)
N=22 (Day 29)

Statistical analyses

No statistical analyses for this end point

Secondary: 8_Spirometry variable -- FEV1 predicted -- from Visit 4 to Visit 11 (Absolute change)

End point title	8_Spirometry variable -- FEV1 predicted -- from Visit 4 to Visit 11 (Absolute change)

End point description:

Spirometry -- FEV1 predicted, from Visit 4 (enrolment) to Visit 11 (last treatment) -- Absolute change

AC=Allergen challenge
FEV1=Forced expiratory volume in 1 second

End point type	Secondary

End point timeframe:

Before allergen challenge (AC) at visit 4 (Day -1, enrolment) and at visit 11 (Day 28, end of treatment).

End point values	SB010	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[15]	19[16]		
Units: litre(s)				
arithmetic mean (standard deviation)	-0.001 (± 0.007)	-0.003 (± 0.008)		

Notes:

[15] - Intention to treat population

[16] - Intention to treat population

Statistical analyses

No statistical analyses for this end point

Secondary: 9_Spirometry variable -- FEV1 predicted -- from Visit 4 to Visit 11 (Percent change)

End point title	9_Spirometry variable -- FEV1 predicted -- from Visit 4 to Visit 11 (Percent change)

End point description:

Spirometry -- FEV1 predicted, from Visit 4 to Visit 11 (Percent change).

AC=Allergen challenge
FEV1=Forced expiratory volume in 1 second

End point type	Secondary

End point timeframe:

Before allergen challenge (AC) at visit 4 (Day -1, enrolment) and at visit 11 (Day 28, end of treatment).

End point values	SB010	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[17]	19[18]		
Units: percent				
arithmetic mean (standard deviation)	-0.032 (± 0.146)	-0.066 (± 0.205)		

Notes:

[17] - Intention to treat population

[18] - Intention to treat population

Statistical analyses

No statistical analyses for this end point

Secondary: 10_Spirometry variable -- FVC predicted -- from Visit 4 to Visit 11 (Absolute change)

End point title	10_Spirometry variable -- FVC predicted -- from Visit 4 to Visit 11 (Absolute change)

End point description:

Spirometry -- FVC predicted, from Visit 4 to Visit 11 (Absolute change).

AC=Allergen challenge
FVC=Forced vital capacity

End point type	Secondary

End point timeframe:

Before allergen challenge (AC) at visit 4 (Day -1, enrolment) and at visit 11 (Day 28, end of treatment).

End point values	SB010	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[19]	19[20]		
Units: litre(s)				
arithmetic mean (standard deviation)	-0.019 (± 0.081)	-0.003 (± 0.009)		

Notes:

[19] - Intention to treat population

[20] - Intention to treat population

Statistical analyses

No statistical analyses for this end point

Secondary: 11_Spirometry variable -- FVC predicted -- from Visit 4 to Visit 11 (Percent change)

End point title	11_Spirometry variable -- FVC predicted -- from Visit 4 to Visit 11 (Percent change)

End point description:

Spirometry -- FVC predicted, from Visit 4 to Visit 11 (Percent change).

AC=Allergen challenge
FVC=Forced vital capacity

End point type	Secondary

End point timeframe:

Before allergen challenge (AC) at visit 4 (Day -1, enrolment) and at visit 11 (Day 28, end of treatment).

End point values	SB010	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[21]	19[22]		
Units: percent				
arithmetic mean (standard deviation)	-0.350 (± 1.521)	-0.065 (± 0.194)		

Notes:

[21] - Intention to treat population

[22] - Intention to treat population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AE) were monitored from the time of signing the informed consent to the end of the study (or study discontinuation). The study duration was from Day -56 (Screening visit) to Day 88 ± 4 (Follow-up visit).

Adverse event reporting additional description:

AEs are presented as treatment-emergent adverse events (TEAE), as safety set.

No serious TEAE was reported during this study.
One non-TEAE serious AE (SAE) occurred about 2 months after the end of treatment period. The SAE was 'detachment of the retina right', with onset 8 weeks after the last dose of study medication; not related to treatment

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	SB010
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	SB010	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	SB010	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 22 (27.27%)	8 / 21 (38.10%)	
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Nervous system disorders			

Headache			
subjects affected / exposed	2 / 22 (9.09%)	2 / 21 (9.52%)	
occurrences (all)	4	2	
Sciatica			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Nasopharyngitis			
subjects affected / exposed	2 / 22 (9.09%)	3 / 21 (14.29%)	
occurrences (all)	2	3	
Dyspnoea			
subjects affected / exposed	0 / 22 (0.00%)	2 / 21 (9.52%)	
occurrences (all)	0	2	
Oropharyngeal pain			
subjects affected / exposed	1 / 22 (4.55%)	1 / 21 (4.76%)	
occurrences (all)	1	1	
Asthma			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Bronchial obstruction			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Increased upper airway secretion			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			

subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Herpes simplex			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25981191