Clinical trial results:
A Randomized, Open-label, Multicenter Study to Evaluate the Effect of Xolair (Omalizumab) as Add-on Therapy to Inhaled Corticosteroid + Long-Acting Beta Agonist in Fixed or Flexible Dosing Compared to Isolated Inhaled Corticosteroid + Long-Acting Beta Agonist in Fixed or Flexible Dosing in the Asthma-Related Quality of Life in Patients With Severe Persistent Allergic Asthma

Summary

EudraCT number	2015-003533-10
Trial protocol	Outside EU/EEA
Global end of trial date	28 April 2010

Results information

Result version number	v1 (current)
This version publication date	06 January 2017
First version publication date	06 January 2017

Trial information

Trial identification

Sponsor protocol code	CIGE025ABR01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00567476
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharmaceuticals AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharmaceuticals 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	28 April 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 April 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The Mean Change From Baseline to Week 20 in the Overall Asthma Quality of Life Questionnaire (AQLQ)

Protection of trial subjects:

Subjects were advised that between visits they could take rescue medication using inhaled salbutamol or terbuline for symptoms of intercurrent bronchospasm. The number of puffs taken during each 24 hours had to be recorded in the subject diary.
If reversibility was going to be assessed, subjects could NOT use their rescue medication within 6 hours of the spirometry, unless severe intercurrent bronchospasm was developed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 November 2007
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	Brazil: 116
Worldwide total number of subjects	116
EEA total number of subjects	0

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)	2
Adults (18-64 years)	105
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects randomized to this study had to meet the GINA guidelines criteria for severe persistent asthma. Current international asthma management guidelines (GINA – Global Initiative for Asthma) advocate the importance of combined pharmacotherapy to control the underlying inflammatory disease and relieve acute symptoms.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Xolair®+ Conventional Therapy

Arm description:

Omalizumab was administered subcutaneously every 2 or 4 weeks over a period of 20 weeks to provide a dose of at least 0.016 mg/kg per UI/ml of immunoglobulin E (IgE). Doses (mg) and dosing frequency were determined by serum total IgE level (IU/mL) and body weight (kg). Also, participants continued using their current formulation of inhaled corticosteroid (ICS) and long-acting beta 2-adrenergic agonist (LABA). Home use of nebulized beta 2-agonist was allowed for the treatment of symptoms of intercurrent bronchospasm or during an asthma exacerbation if this treatment regimen was already established prior to screening visit.

Arm type	Active comparator
Investigational medicinal product name	Xolair®
Investigational medicinal product code	
Other name	Omalizumab
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Omalizumab 150 to 375 mg was administered subcutaneously every 2 or 4 weeks to provide a dose of at least 0.016 mg/kg per UI/ml of IgE.

Investigational medicinal product name	Inhaled corticosteroids (ICS)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use

Dosage and administration details:

Any ICS with proprietary drug and device > 500 mcg of fluticasone or equivalent.

Investigational medicinal product name	Long-acting beta 2-adrenergic agonist (LABA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Fixed dose of LABA as prescribed prior to study entry

Investigational medicinal product name	Short-acting beta 2-adrenergic agonist (SABA)
Investigational medicinal product code	
Other name	salbutamol, terbutaline
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

Home use of nebulized B2-agonist such as salbutamol 5 mg or terbutaline 10 mg for symptoms of intercurrent bronchospasm.

Arm title	Conventional Therapy

Arm description:

Participants continued using their current formulation of inhaled corticosteroid (ICS) and a long-acting beta 2-adrenergic agonist (LABA). Home use of nebulized beta 2-agonist was allowed for the treatment of symptoms of intercurrent bronchospasm or during an asthma exacerbation if this treatment regimen was already established prior to screening visit.

Arm type	Active comparator
Investigational medicinal product name	Inhaled corticosteroids (ICS)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use

Dosage and administration details:

Any ICS with proprietary drug and device > 500 mcg of fluticasone or equivalent.

Investigational medicinal product name	Long-acting beta 2-adrenergic agonist (LABA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Fixed dose of LABA as prescribed prior to study entry

Investigational medicinal product name	Short-acting beta 2-adrenergic agonist (SABA)
Investigational medicinal product code	
Other name	salbutamol, terbutaline
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

Home use of nebulized B2-agonist such as salbutamol 5 mg or terbutaline 10 mg for symptoms of intercurrent bronchospasm.

Number of subjects in period 1	Xolair®+ Conventional Therapy	Conventional Therapy
Started	78	38
Completed	70	34
Not completed	8	4
Administrative issues	1	-
Adverse event, non-fatal	2	-
Significant protocol violation	4	1
Withdrew because of medical decision	-	1

Pregnancy	1	-
Lost to follow-up	-	1
No adherence to the protocol	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Xolair®+ Conventional Therapy
Reporting group description:	
Omalizumab was administered subcutaneously every 2 or 4 weeks over a period of 20 weeks to provide a dose of at least 0.016 mg/kg per UI/ml of immunoglobulin E (IgE). Doses (mg) and dosing frequency were determined by serum total IgE level (IU/mL) and body weight (kg). Also, participants continued using their current formulation of inhaled corticosteroid (ICS) and long-acting beta 2-adrenergic agonist (LABA). Home use of nebulized beta 2-agonist was allowed for the treatment of symptoms of intercurrent bronchospasm or during an asthma exacerbation if this treatment regimen was already established prior to screening visit.	
Reporting group title	Conventional Therapy
Reporting group description:	
Participants continued using their current formulation of inhaled corticosteroid (ICS) and a long-acting beta 2-adrenergic agonist (LABA). Home use of nebulized beta 2-agonist was allowed for the treatment of symptoms of intercurrent bronchospasm or during an asthma exacerbation if this treatment regimen was already established prior to screening visit.	

Reporting group values	Xolair®+ Conventional Therapy	Conventional Therapy	Total
Number of subjects	78	38	116
Age categorical Units: Subjects			
Adolescents (12-17 years)	1	1	2
Adults (18-64 years)	72	33	105
From 65-84 years	5	4	9
Age continuous Units: years			
arithmetic mean	43.8	45.2	
standard deviation	± 13.1	± 12.8	-
Gender categorical Units: Subjects			
Female	60	29	89
Male	18	9	27

End points

End points reporting groups

Reporting group title	Xolair®+ Conventional Therapy

Reporting group description:

Omalizumab was administered subcutaneously every 2 or 4 weeks over a period of 20 weeks to provide a dose of at least 0.016 mg/kg per UI/ml of immunoglobulin E (IgE). Doses (mg) and dosing frequency were determined by serum total IgE level (IU/mL) and body weight (kg). Also, participants continued using their current formulation of inhaled corticosteroid (ICS) and long-acting beta 2-adrenergic agonist (LABA). Home use of nebulized beta 2-agonist was allowed for the treatment of symptoms of intercurrent bronchospasm or during an asthma exacerbation if this treatment regimen was already established prior to screening visit.

Reporting group title	Conventional Therapy

Reporting group description:

Participants continued using their current formulation of inhaled corticosteroid (ICS) and a long-acting beta 2-adrenergic agonist (LABA). Home use of nebulized beta 2-agonist was allowed for the treatment of symptoms of intercurrent bronchospasm or during an asthma exacerbation if this treatment regimen was already established prior to screening visit.

Primary: The Mean Change From Baseline to Week 20 in the Overall Asthma Quality of Life Questionnaire (AQLQ)

End point title	The Mean Change From Baseline to Week 20 in the Overall Asthma Quality of Life Questionnaire (AQLQ)[1]

End point description:

The AQLQ was administered to all patients at Baseline, Week 12 and Week 20. The 32 questions in the AQLQ were divided into four domains; activity limitations, symptoms, emotional function, and environmental stimuli. Individual questions are equally weighted. The overall AQLQ score is the mean of the responses to each of the 32 questions, and ranges from 1 to 7. A score 7.0 indicates that the patient has no impairments due to asthma and a score of 1.0 indicates severe impairment.

End point type	Primary

End point timeframe:

Baseline and Week 20

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis provided for this primary end point.

End point values	Xolair®+ Conventional Therapy	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78[2]	38		
Units: Units on a scale				
arithmetic mean (standard error)				
Baseline (n=77, 37)	3.1 (± 1)	3.1 (± 1.1)		
At Week 20 (n=78, 36)	4.4 (± 1.4)	3 (± 1.1)		
Change from baseline to week 20 (n=77, 36)	1.2 (± 0.1)	-0.1 (± 0.1)		

Notes:

[2] - intent-to treat (ITT) population- 1 dose of study drug and 1 post-baseline safety/efficacy assesment

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With an Increase of More Than 1.5 in AQLQ Overall Score at 20 Weeks

End point title	Percentage of Participants With an Increase of More Than 1.5 in AQLQ Overall Score at 20 Weeks

End point description:

The AQLQ was administered to all patients at Baseline, Week 12 and Week 20. The 32 questions in the AQLQ were divided into four domains; activity limitations, symptoms, emotional function, and environmental stimuli. Individual questions are equally weighted. The overall AQLQ score is the mean of the responses to each of the 32 questions and ranges from 1 to 7. A score 7.0 indicates that the patient has no impairments due to asthma and score 1.0 indicates severe impairment.

End point type	Secondary

End point timeframe:

Baseline and Week 20

End point values	Xolair®+ Conventional Therapy	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77[3]	36		
Units: Percentage of participants				
number (confidence interval 95%)	40.3 (30 to 51.4)	2.8 (0.5 to 14.2)		

Notes:

[3] - intent-to treat (ITT) population- 1 dose of study drug and 1 post-baseline safety/efficacyassesment

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With an Increase of More Than 0.5 in AQLQ Overall Score at Week 20

End point title	Percentage of Participants With an Increase of More Than 0.5 in AQLQ Overall Score at Week 20

End point description:

The AQLQ was administered to all patients at Baseline, Week 12 and Week 20. The 32 questions in the AQLQ were divided into four domains; activity limitations, symptoms, emotional function, and environmental stimuli. Individual questions are equally weighted. The overall AQLQ score is the mean of the responses to each of the 32 questions and ranges from 1 to 7. AQLQ of each domain is the mean of the responses to each of the questions within that domain. A score 7.0 indicates that the patient has no impairments due to asthma and score 1.0 indicates severe impairment.

End point type	Secondary

End point timeframe:

Baseline and Week 20

End point values	Xolair®+ Conventional Therapy	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77[4]	36		
Units: Percentage of participants				
number (confidence interval 95%)	70.1 (59.2 to 79.2)	22.2 (11.7 to 38.1)		

Notes:

[4] - intent-to treat (ITT) population- 1 dose of study drug and 1 post-baseline safety/efficacy assesment

Statistical analyses

No statistical analyses for this end point

Secondary: The Mean Change From Baseline to the End of Study in AQLQ Domain Score

End point title	The Mean Change From Baseline to the End of Study in AQLQ Domain Score

End point description:

AQLQ was administered to all patients at Baseline, Week 12 and Week 20, and prior to any clinic visit evaluation and drug administration.
The 32 questions in the AQLQ were divided into four domains: activity limitations, symptoms, emotional function, and environmental stimuli. AQLQ domain scores were calculated by adding the responses to each of the questions in the domain and dividing by the number of questions in the domain. Each domain score was between 1 and 7. Score 7.0 meant that the patient had no impairments due to asthma and score 1.0 indicated severe impairment.

End point type	Secondary

End point timeframe:

Baseline and Week 20

End point values	Xolair®+ Conventional Therapy	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78[5]	38		
Units: Units on a scale				
arithmetic mean (standard error)				
Activity limitation score	1.3 (± 0.1)	-0.2 (± 0.1)		
Symptoms score	1.2 (± 0.2)	-0.2 (± 0.2)		
Emotional function score	1.3 (± 0.2)	0 (± 0.1)		
Environmental stimuli score	1.2 (± 0.2)	0 (± 0.2)		

Notes:

[5] - intent-to treat (ITT) population- 1 dose of study drug and 1 post-baseline safety/efficacy assesment

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Asthma Exacerbation Episodes Per Participant

End point title	Number of Asthma Exacerbation Episodes Per Participant

End point description:

For the purpose of evaluating efficacy, a clinically significant asthma exacerbation was defined as a worsening of asthma symptoms as judged clinically by the investigator, requiring doubling the baseline ICS dose for at least 3 days and/or treatment with rescue systemic (oral or IV) corticosteroids. The initiation of the above corticosteroid regimens marked the start of an asthma exacerbation episode and cessation of the additional corticosteroid regimens marked the end of an exacerbation episode.

End point type	Secondary

End point timeframe:

From Baseline through 20 weeks

End point values	Xolair®+ Conventional Therapy	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78[6]	38		
Units: Participants				
number (not applicable)				
Patients with 1 episode	25	12		
Patients with 2 episodes	5	6		
Patients with 3 episodes	3	1		
Patients with 4 episodes	1	1		
Total number of patients with episodes	34	20		

Notes:

[6] - intent-to treat (ITT) population- 1 dose of study drug and 1 post-baseline safety/efficacy assesment

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Using Rescue Medication

End point title	Percentage of Participants Using Rescue Medication

End point description:

When necessary, patients were allowed to take rescue medication using inhaled salbutamol or terbutaline for symptoms of intercurrent bronchospasm.

End point type	Secondary

End point timeframe:

From Baseline through 20 Weeks

End point values	Xolair®+ Conventional Therapy	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78[7]	38		
Units: Percentage of participants				
number (confidence interval 95%)	43.6 (33.1 to 54.6)	44.7 (30.1 to 60.3)		

Notes:

[7] - intent-to treat (ITT) population- 1 dose of study drug and 1 post-baseline safety/efficacy assesment

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Number of Puffs of Rescue Medication Taken Per Day

End point title	Mean Number of Puffs of Rescue Medication Taken Per Day

End point description:

When necessary, patients were allowed to take rescue medication using inhaled salbutamol or terbutaline for symptoms of intercurrent bronchospasm. The number of puffs taken during each 24 hour period was recorded in the patient dairy. The total number of puffs over 20 weeks of treatment was divided by the number of treatment days (140 days) to calculate the mean number of puffs per day.

End point type	Secondary

End point timeframe:

From Baseline through 20 Weeks

End point values	Xolair®+ Conventional Therapy	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34[8]	17		
Units: Puffs				
arithmetic mean (standard deviation)	5.5 (± 4.1)	6.4 (± 4.7)		

Notes:

[8] - intent-to treat (ITT) population- 1 dose of study drug and 1 post-baseline safety/efficacy assesment

Statistical analyses

No statistical analyses for this end point

Secondary: Physician's Global Assessment of Treatment Effectiveness

End point title	Physician's Global Assessment of Treatment Effectiveness

End point description:

At the end of Week 20 a global evaluation of the treatment effectiveness was performed by the investigator using the following scale: Excellent: complete control of asthma; Good: marked improvement of asthma; Moderate: discernible, but limited improvement in asthma; Poor: no appreciable change in asthma; Worsening of asthma

End point type	Secondary

End point timeframe:

20 Weeks

End point values	Xolair®+ Conventional Therapy	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76[9]	37		
Units: Participants				
number (not applicable)				
Excellent	22	2		
Good	35	4		
Moderate	13	11		
Poor	6	18		
Worsening	0	2		

Notes:

[9] - intent-to treat (ITT) population- 1 dose of study drug and 1 post-baseline safety/efficacy assesment

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's Global Assessment of Treatment Effectiveness

End point title	Patient's Global Assessment of Treatment Effectiveness

End point description:

At the end of Week 20, a global evaluation of the treatment effectiveness was performed by the patient using the following scale:
Excellent: complete control of asthma; Good: marked improvement of asthma; Moderate: discernible, but limited improvement in asthma; Poor: no appreciable change in asthma; Worsening of asthma.

End point type	Secondary

End point timeframe:

20 Weeks

End point values	Xolair®+ Conventional Therapy	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76[10]	37		
Units: Participants				
number (not applicable)				
Excellent	33	3		
Good	30	13		
Moderate	10	10		
Poor	3	9		
Worsening	0	2		

Notes:

[10] - intent-to treat (ITT) population- 1 dose of study drug and 1 post-baseline safety/efficacy assesment

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Free Days With no Rescue Medication

End point title	Free Days With no Rescue Medication

End point description:

When necessary, patients were allowed to take rescue medication using inhaled salbutamol or terbutaline for symptoms of intercurrent bronchospasm. Days with no rescue medication intake were the variable of interest for this analysis.

End point type	Other pre-specified

End point timeframe:

From Baseline through 20 weeks (140 days)

End point values	Xolair®+ Conventional Therapy	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78[11]	38		
Units: Days				
arithmetic mean (standard deviation)	73.5 (± 39.4)	74.9 (± 35.4)		

Notes:

[11] - intent-to treat (ITT) population- 1 dose of study drug and 1 post-baseline safety/efficacy assesment

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	13.0

Reporting groups

Reporting group title	XOLAIR® +LABA + ICS

Reporting group description:

XOLAIR® +LABA + ICS

Reporting group title	LABA + ICS

Reporting group description:

LABA + ICS

Serious adverse events	XOLAIR® +LABA + ICS	LABA + ICS	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 78 (3.85%)	0 / 38 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 78 (1.28%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonia			
subjects affected / exposed	1 / 78 (1.28%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 78 (1.28%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	XOLAIR® +LABA + ICS	LABA + ICS	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 78 (53.85%)	16 / 38 (42.11%)	
Injury, poisoning and procedural complications			
Joint sprain			
subjects affected / exposed	4 / 78 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	4	0	
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 78 (20.51%)	4 / 38 (10.53%)	
occurrences (all)	39	9	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 78 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	4	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 78 (1.28%)	2 / 38 (5.26%)	
occurrences (all)	2	4	
Respiratory, thoracic and mediastinal disorders			
Nasopharyngitis			
subjects affected / exposed	6 / 78 (7.69%)	0 / 38 (0.00%)	
occurrences (all)	6	0	
Respiratory tract infection			
subjects affected / exposed	8 / 78 (10.26%)	3 / 38 (7.89%)	
occurrences (all)	9	3	
Rhinitis			
subjects affected / exposed	3 / 78 (3.85%)	4 / 38 (10.53%)	
occurrences (all)	8	4	
Rhinitis allergic			

subjects affected / exposed	1 / 78 (1.28%)	2 / 38 (5.26%)	
occurrences (all)	2	2	
Sinusitis			
subjects affected / exposed	10 / 78 (12.82%)	2 / 38 (5.26%)	
occurrences (all)	11	2	
Upper respiratory tract infection			
subjects affected / exposed	5 / 78 (6.41%)	3 / 38 (7.89%)	
occurrences (all)	5	3	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	5 / 78 (6.41%)	2 / 38 (5.26%)	
occurrences (all)	7	4	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 78 (5.13%)	1 / 38 (2.63%)	
occurrences (all)	4	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	8 / 78 (10.26%)	1 / 38 (2.63%)	
occurrences (all)	9	1	

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