



Clinical trial results:

A randomised, multi-centre, parallel group, double-blind, placebo-controlled study to assess the efficacy and safety of Oscillococcinum® in the treatment of symptoms of Influenza-like illness (ILI)

Summary

EudraCT number	2013-001869-16
Trial protocol	DE
Global end of trial date	19 May 2014

Results information

Result version number	v1 (current)
This version publication date	08 July 2022
First version publication date	08 July 2022
Summary attachment (see zip file)	Prematurely ended statement (Prematurely ended statement.pdf)

Trial information

Trial identification

Sponsor protocol code	BRN-C-2013-02
-----------------------	---------------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Boiron Laboratoires
Sponsor organisation address	2 avenue de l'Ouest Lyonnais, Messimy, France, 69510
Public contact	Isabelle Chanel - Research and Development Director, Boiron Laboratoires, +33 4 72 16 43 15, isabelle.chanel@boiron.fr
Scientific contact	Isabelle Chanel - Research and Development Director, Boiron Laboratoires, +33 4 72 16 43 15, isabelle.chanel@boiron.fr

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	10 February 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 May 2014
Global end of trial reached?	Yes
Global end of trial date	19 May 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the efficacy of Oscilloccoccinum® in the treatment of symptoms of Influenza-like illness (ILI).

Protection of trial subjects:

The Sponsor submitted the study protocol and all information necessary for a detailed review of the clinical study to the competent authority. The study was started after written approval by the competent authority was available.

This study was performed in accordance with Good Clinical Practice (GCP), the Declaration of Helsinki, in its revision of Somerset West 1996, and in accordance with applicable legal and regulatory requirements, including archiving of essential documents.

It was the responsibility of the investigator to obtain signed informed consent from the patient prior to the patient's inclusion in the study. For patients under 18 years of age, the investigator was obliged to collect signed informed consent not only from the patient, but also from the patient's parents.

Background therapy:

-

Evidence for comparator:

-

Actual start date of recruitment	05 November 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 362
Worldwide total number of subjects	362
EEA total number of subjects	362

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)	8
Adults (18-64 years)	354
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients with ILI defined as sudden onset of symptoms and at least 1 of the systemic symptoms and at least 1 of the respiratory symptoms of ≤ 24 hours duration were recruited.

Patients were randomized at a rate of 1:1 to receive either Oscillococcinum® or placebo, randomization was stratified in 2 strata depending the symptom scores.

Pre-assignment

Screening details:

362 patients were enrolled, 351 patients were randomized, 2 patient randomized were not treated. A total of 110 patients (30.4%) was enrolled with baseline total symptom score B 2 - 8 comprising Stratum 1 and 249 patients (68.8%) with baseline total symptom score B ≥ 9 in Stratum 2.

Treatment groups were balanced in baseline characteristics.

Pre-assignment period milestones

Number of subjects started	362
Number of subjects completed	349

Pre-assignment subject non-completion reasons

Reason: Number of subjects	patient non randomized non treated: 8
Reason: Number of subjects	patient non randomized treated: 3
Reason: Number of subjects	patients randomized non treated: 2

Period 1

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

Blinding implementation details:

Study medication was presented as visually indistinguishable doses. Each carton box contained 10 doses which was sufficient medication for 1 patient.

Sealed individual random code envelopes were prepared for the purpose of individual unblinding of a patient's treatment allocation. These envelopes were sent to the sites together with the study medication.

Arms

Are arms mutually exclusive?	Yes
Arm title	Oscillococcinum®

Arm description:

Oscillococcinum® was provided as globuli with 1 dose containing 1 g of globuli.

Oscillococcinum® contained the extract from Anas barbariae, hepatis and cordis 200K, 0.85 g sucrose, and 0.15 g lactose.

Oscillococcinum® were to be taken as 3 oral doses per day over 3 days.

Arm type	Experimental
----------	--------------

Investigational medicinal product name	Oscillococcinum®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules in single-dose container
Routes of administration	Oral use

Dosage and administration details:

Oscillococcinum® was to be taken as 3 oral doses per day over 3 days. The entire content of 1 dose was to let melt under the tongue.

Patients were to be instructed to take all 9 doses as scheduled even if they were free of symptoms.

Arm title	Placebo
------------------	---------

Arm description:

Placebo were provided as globuli with 1 dose containing 1 g of globuli.

Placebo contained 0.85 g sucrose and 0.15 g lactose and it was not possible to differentiate it from Oscillococcinum® by its appearance and taste.

Placebo were to be taken as 3 oral doses per day over 3 days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules in single-dose container
Routes of administration	Oral use

Dosage and administration details:

Placebo were provided as globuli with 1 dose containing 1 g of globuli.

Placebo contained 0.85 g sucrose and 0.15 g lactose and it was not possible to differentiate it from Oscillococcinum® by its appearance and taste.

Number of subjects in period 1^[1]	Oscillococcinum®	Placebo
Started	175	174
Completed	159	155
Not completed	16	19
Consent withdrawn by subject	-	5
Adverse event, non-fatal	3	1
Other	2	1
Lack of compliance	10	10
Lost to follow-up	1	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: For the final analysis, 362 patients were enrolled, and 349 patients were included in the efficacy analysis (FAS), representing an overrun of 108 patients compared to the number of patients included in the first interim analysis.

A total of 351 patients (97.0 %) was randomised, 175 patients (49.9 %) to Oscillococcinum treatment and 176 patients (50.1 %) to placebo treatment. (see Pre-assignment subject non-completion reasons above)

Baseline characteristics

Reporting groups

Reporting group title	Oscillococcinum®
-----------------------	------------------

Reporting group description:

Oscillococcinum® was provided as globuli with 1 dose containing 1 g of globuli. Oscillococcinum® contained the extract from *Anas barbariae*, *hepatis* and *cordis* 200K, 0.85 g sucrose, and 0.15 g lactose. Oscillococcinum® were to be taken as 3 oral doses per day over 3 days.

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

Placebo were provided as globuli with 1 dose containing 1 g of globuli. Placebo contained 0.85 g sucrose and 0.15 g lactose and it was not possible to differentiate it from Oscillococcinum® by its appearance and taste. Placebo were to be taken as 3 oral doses per day over 3 days.

Reporting group values	Oscillococcinum®	Placebo	Total
Number of subjects	175	174	349
Age categorical			
Age of subjects (years)			
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)	3	5	8
Adults (18-64 years)	172	169	341
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Mean age of subjects SD (years)			
Units: years			
arithmetic mean	37.5	37.6	
standard deviation	± 12.8	± 12.6	-
Gender categorical			
Units: Subjects			
Female	85	86	171
Male	90	88	178

Subject analysis sets

Subject analysis set title	Stratum 1 - Oscillococcinum
----------------------------	-----------------------------

Subject analysis set type	Sub-group analysis
---------------------------	--------------------

Subject analysis set description:

Randomization to treatment group was stratified according to the total symptom scores at baseline. Patients with a total symptom score version 1 calculated from the baseline symptom score B between 2 and 8, inclusively received Oscillococcinum

Subject analysis set title	Stratum 1 - Placebo
----------------------------	---------------------

Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Randomization to treatment group was stratified according to the total symptom scores at baseline. Patients with a total symptom score version 1 calculated from the baseline symptom score B between 2 and 8, inclusively received placebo	
Subject analysis set title	Stratum 2 - Oscillocoquinum
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Randomization to treatment group was stratified according to the total symptom scores at baseline. Patients with a total symptom score version 1 calculated from the baseline symptom score B of 9 or higher receiving Oscillocoquinum	
Subject analysis set title	Stratum 2 - Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Randomization to treatment group was stratified according to the total symptom scores at baseline. Patients with a total symptom score version 1 calculated from the baseline symptom score B of 9 or higher received placebo	

Reporting group values	Stratum 1 - Oscillocoquinum	Stratum 1 - Placebo	Stratum 2 - Oscillocoquinum
Number of subjects	52	55	123
Age categorical			
Age of subjects (years)			
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)	3	4	0
Adults (18-64 years)	49	51	123
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Mean age of subjects SD (years)			
Units: years			
arithmetic mean	35.2	35.7	38.4
standard deviation	± 12.5	± 13.8	± 12.9
Gender categorical			
Units: Subjects			
Female	25	28	60
Male	27	27	63

Reporting group values	Stratum 2 - Placebo		
Number of subjects	119		
Age categorical			
Age of subjects (years)			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		

Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	1		
Adults (18-64 years)	118		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Mean age of subjects SD (years)			
Units: years			
arithmetic mean	38.5		
standard deviation	± 12.0		
Gender categorical			
Units: Subjects			
Female	58		
Male	61		

End points

End points reporting groups

Reporting group title	Oscillococcinum®
-----------------------	------------------

Reporting group description:

Oscillococcinum® was provided as globuli with 1 dose containing 1 g of globuli.
Oscillococcinum® contained the extract from *Anas barbariae*, *hepatis* and *cordis* 200K, 0.85 g sucrose, and 0.15 g lactose.
Oscillococcinum® were to be taken as 3 oral doses per day over 3 days.

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

Placebo were provided as globuli with 1 dose containing 1 g of globuli.
Placebo contained 0.85 g sucrose and 0.15 g lactose and it was not possible to differentiate it from Oscillococcinum® by its appearance and taste.
Placebo were to be taken as 3 oral doses per day over 3 days.

Subject analysis set title	Stratum 1 - Oscillococcinum
----------------------------	-----------------------------

Subject analysis set type	Sub-group analysis
---------------------------	--------------------

Subject analysis set description:

Randomization to treatment group was stratified according to the total symptom scores at baseline. Patients with a total symptom score version 1 calculated from the baseline symptom score B between 2 and 8, inclusively received Oscillococcinum

Subject analysis set title	Stratum 1 - Placebo
----------------------------	---------------------

Subject analysis set type	Sub-group analysis
---------------------------	--------------------

Subject analysis set description:

Randomization to treatment group was stratified according to the total symptom scores at baseline. Patients with a total symptom score version 1 calculated from the baseline symptom score B between 2 and 8, inclusively received placebo

Subject analysis set title	Stratum 2 - Oscillococcinum
----------------------------	-----------------------------

Subject analysis set type	Sub-group analysis
---------------------------	--------------------

Subject analysis set description:

Randomization to treatment group was stratified according to the total symptom scores at baseline. Patients with a total symptom score version 1 calculated from the baseline symptom score B of 9 or higher receiving Oscillococcinum

Subject analysis set title	Stratum 2 - Placebo
----------------------------	---------------------

Subject analysis set type	Sub-group analysis
---------------------------	--------------------

Subject analysis set description:

Randomization to treatment group was stratified according to the total symptom scores at baseline. Patients with a total symptom score version 1 calculated from the baseline symptom score B of 9 or higher received placebo

Primary: Primary endpoint -Time to absence of systemic flu-like symptoms

End point title	Primary endpoint -Time to absence of systemic flu-like symptoms
-----------------	---

End point description:

Time from first intake of study medication to the first occurrence of no fever (body temperature < 37.8°C) AND chills, headache, myalgia, and malaise recorded as 'none'. Scores of 'none' for fever, chills, headache, myalgia, and malaise had to be maintained over 24 hours.
Median time will be compared between treatment groups.

End point type	Primary
----------------	---------

End point timeframe:

4 days follow up

End point values	Oscillococcinu m®	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	174		
Units: hours				
number (not applicable)	138.3	148.4		

Statistical analyses

Statistical analysis title	Primary endpoint FAS
Statistical analysis description:	
Full analysis set	
Comparison groups	Oscillococcinum® v Placebo
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4846
Method	Chi-squared

Primary: Primary endpoint PP Time to absence of systemic flu-like symptoms

End point title	Primary endpoint PP Time to absence of systemic flu-like symptoms
End point description:	
Time from first intake of study medication to the first occurrence of no fever (body temperature < 37.8°C) AND chills, headache, myalgia, and malaise recorded as 'none'. Scores of 'none' for fever, chills, headache, myalgia, and malaise had to be maintained over 24 hours.	
Median time compared for treatment groups	
End point type	Primary
End point timeframe:	
4 days follow up	

End point values	Oscillococcinu m®	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	138		
Units: hours				
number (not applicable)	121.8	134.4		

Statistical analyses

Statistical analysis title	Primary endpoint PP
Statistical analysis description:	
Per protocol population	

Comparison groups	Oscillococcinum® v Placebo
Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4799
Method	Chi-squared

Primary: Primary endpoint Stratum 1

End point title	Primary endpoint Stratum 1
End point description: Time from first intake of study medication to the first occurrence of no fever (body temperature < 37.8°C) AND chills, headache, myalgia, and malaise recorded as 'none'. Scores of 'none' for fever, chills, headache, myalgia, and malaise had to be maintained over 24 hours. Comparison of median time between patients data of stratum 1 randomized to Oscillococcinum or Placebo group.	
End point type	Primary
End point timeframe: 4 day follow up	

End point values	Stratum 1 - Oscillococcinum	Stratum 1 - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	52	55		
Units: hours				
number (not applicable)	90.3	117.5		

Statistical analyses

Statistical analysis title	Primary endpoint Stratum 1
Statistical analysis description: Full analysis set for patients in Stratum 1	
Comparison groups	Stratum 1 - Oscillococcinum v Stratum 1 - Placebo
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0567
Method	Chi-squared

Primary: Primary endpoint Stratum 2

End point title	Primary endpoint Stratum 2
End point description: Time from first intake of study medication to the first occurrence of no fever (body temperature < 37.8°	

C) AND chills, headache, myalgia, and malaise recorded as 'none'. Scores of 'none' for fever, chills, headache, myalgia, and malaise had to be maintained over 24 hours.

Comparison of median time between patients data of stratum 2 randomized to Oscillocochinum or Placebo group.

End point type	Primary
End point timeframe:	
4 days follow up	

End point values	Stratum 2 - Oscillocochinum	Stratum 2 - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	123	119		
Units: hours				
number (not applicable)	0	175		

Statistical analyses

Statistical analysis title	Primary endpoint Stratum 2
Statistical analysis description:	
Full analysis set	
Comparison groups	Stratum 2 - Oscillocochinum v Stratum 2 - Placebo
Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.506 ^[1]
Method	Chi-squared

Notes:

[1] - Median time to absence of systemic flu-like symptoms (h) value for Stratum 2 Oscillocochinum group is reported as "0" in the above tabulated results, since it could not be determined in the follow up time.

Primary: Primary endpoint Stratum 1 - PP

End point title	Primary endpoint Stratum 1 - PP
End point description:	
Time from first intake of study medication to the first occurrence of no fever (body temperature < 37.8°C) AND chills, headache, myalgia, and malaise recorded as 'none'. Scores of 'none' for fever, chills, headache, myalgia, and malaise had to be maintained over 24 hours.	
Comparison of median time between patients data of stratum 1 randomized to Oscillocochinum or Placebo group.	
End point type	Primary
End point timeframe:	
4 day follow up	

End point values	Stratum 1 - Oscillocochinu m	Stratum 1 - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	45		
Units: hours				
number (not applicable)	89.2	113.5		

Statistical analyses

Statistical analysis title	Primary endpoint Stratum 1 PP
Comparison groups	Stratum 1 - Oscillocochinum v Stratum 1 - Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0359
Method	Chi-squared

Primary: Primary endpoint Stratum 2 - PP

End point title	Primary endpoint Stratum 2 - PP
End point description:	
Time from first intake of study medication to the first occurrence of no fever (body temperature < 37.8°C) AND chills, headache, myalgia, and malaise recorded as 'none'. Scores of 'none' for fever, chills, headache, myalgia, and malaise had to be maintained over 24 hours.	
Comparison of median time between patients data of stratum 2 randomized to Oscillocochinum or Placebo group.	
End point type	Primary
End point timeframe:	
4 days follow up	

End point values	Stratum 2 - Oscillocochinu m	Stratum 2 - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	95	93		
Units: hours				
number (not applicable)	190.5	148.4		

Statistical analyses

Statistical analysis title	Primary endpoint Stratum 2 PP
Comparison groups	Stratum 2 - Oscillocochinum v Stratum 2 - Placebo

Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4007
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:

4 days follow up

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	16.1
--------------------	------

Reporting groups

Reporting group title	Oscillococcinum
-----------------------	-----------------

Reporting group description: -

Reporting group title	Placebo
-----------------------	---------

Reporting group description: -

Serious adverse events	Oscillococcinum	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 176 (0.57%)	0 / 176 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Bronchitis	Additional description: Patient with bronchitis and sinusitis		
subjects affected / exposed	1 / 176 (0.57%)	0 / 176 (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: 0 %

Non-serious adverse events	Oscillococcinum	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 176 (11.36%)	19 / 176 (10.80%)	
Investigations			
Legionella test positive			
subjects affected / exposed	2 / 176 (1.14%)	1 / 176 (0.57%)	
occurrences (all)	2	1	
Body temperature decreased			
subjects affected / exposed	0 / 176 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	

Nervous system disorders			
	Dizziness		
	subjects affected / exposed	0 / 176 (0.00%)	1 / 176 (0.57%)
	occurrences (all)	0	1
	Hypoaesthesia		
	subjects affected / exposed	0 / 176 (0.00%)	1 / 176 (0.57%)
	occurrences (all)	0	1
General disorders and administration site conditions			
	Influenza like illness		
	subjects affected / exposed	2 / 176 (1.14%)	2 / 176 (1.14%)
	occurrences (all)	2	2
	Sensation of foreign body		
	subjects affected / exposed	0 / 176 (0.00%)	1 / 176 (0.57%)
	occurrences (all)	0	1
Ear and labyrinth disorders			
	Ear pain		
	subjects affected / exposed	1 / 176 (0.57%)	1 / 176 (0.57%)
	occurrences (all)	1	1
	Tinnitus		
	subjects affected / exposed	0 / 176 (0.00%)	1 / 176 (0.57%)
	occurrences (all)	0	1
	Vertigo		
	subjects affected / exposed	1 / 176 (0.57%)	0 / 176 (0.00%)
	occurrences (all)	1	0
Eye disorders			
	Conjunctivitis		
	subjects affected / exposed	0 / 176 (0.00%)	1 / 176 (0.57%)
	occurrences (all)	0	1
Gastrointestinal disorders			
	Diarrhoea		
	subjects affected / exposed	1 / 176 (0.57%)	2 / 176 (1.14%)
	occurrences (all)	1	2
	Flatulence		
	subjects affected / exposed	1 / 176 (0.57%)	2 / 176 (1.14%)
	occurrences (all)	1	2
	Gastrooesophageal reflux disease		

subjects affected / exposed occurrences (all)	2 / 176 (1.14%) 2	0 / 176 (0.00%) 0	
Toothache subjects affected / exposed occurrences (all)	1 / 176 (0.57%) 1	1 / 176 (0.57%) 1	
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 176 (0.57%) 1	0 / 176 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	0 / 176 (0.00%) 0	1 / 176 (0.57%) 1	
Dry mouth subjects affected / exposed occurrences (all)	0 / 176 (0.00%) 0	1 / 176 (0.57%) 1	
Gastrointestinal hypomotility subjects affected / exposed occurrences (all)	1 / 176 (0.57%) 1	0 / 176 (0.00%) 0	
Mucous stools subjects affected / exposed occurrences (all)	0 / 176 (0.00%) 0	1 / 176 (0.57%) 1	
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	0 / 176 (0.00%) 0	1 / 176 (0.57%) 1	
Skin and subcutaneous tissue disorders Hyperhidrosis subjects affected / exposed occurrences (all)	1 / 176 (0.57%) 1	1 / 176 (0.57%) 1	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 176 (0.57%) 1	2 / 176 (1.14%) 2	
Back pain subjects affected / exposed occurrences (all)	1 / 176 (0.57%) 1	1 / 176 (0.57%) 1	
Myalgia			

subjects affected / exposed	1 / 176 (0.57%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	0 / 176 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 176 (1.14%)	3 / 176 (1.70%)	
occurrences (all)	2	3	
Sinusitis			
subjects affected / exposed	3 / 176 (1.70%)	1 / 176 (0.57%)	
occurrences (all)	3	1	
Otitis media			
subjects affected / exposed	1 / 176 (0.57%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Pertussis			
subjects affected / exposed	1 / 176 (0.57%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Sinobronchitis			
subjects affected / exposed	1 / 176 (0.57%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	0 / 176 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Herpes zoster			
subjects affected / exposed	0 / 176 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Oral herpes			
subjects affected / exposed	0 / 176 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	0 / 176 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Sinusitis bacterial			
subjects affected / exposed	0 / 176 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2013	Amendment 2; included minor formal corrections, changes and clarifications regarding study variables, addition of two new variables, a modification of the statistical analysis of the primary efficacy endpoint, a detailed definition of the process of obtaining informed consent for children.

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 trial was prematurely terminated following the first previewed interim analysis for futility.

Notes: