



Clinical trial results:

A Phase IV, Open Label, Multi-Centre Study to Evaluate the Safety and Tolerability of CSL Limited's Influenza Virus Vaccine in a Paediatric Population Aged greater than or equal to 6 months to less than 18 years Summary

EudraCT number	2014-004131-40
Trial protocol	Outside EU/EEA
Global end of trial date	22 February 2010

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	30 July 2015

Trial information

Trial identification

Sponsor protocol code	CSLCT-USF-06-29
-----------------------	-----------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00825162
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CSL Limited
Sponsor organisation address	45 Poplar Road, Parkville, Australia, 3052
Public contact	Clinical Program Director, bioCSL, bioCSL PTY LTD, biocsl.clinicaltrials@biocsl.com.au
Scientific contact	Clinical Program Director, bioCSL, bioCSL PTY LTD, biocsl.clinicaltrials@biocsl.com.au

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 April 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 February 2010
Global end of trial reached?	Yes
Global end of trial date	22 February 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Safety and tolerability of CSL Limited's Influenza Virus Vaccine (CSL's IVV) in a pediatric population aged 6 months to less than 18 years.

Protection of trial subjects:

The study protocol, the Participant Information Sheet (PIS), the Informed Consent Form (ICF) and any other written information provided to the participant were reviewed and approved by an Independent Ethics Committee (IEC) at each study site.

This study was conducted in accordance with the standards of Good Clinical Practice, as defined by the International Conference on Harmonisation, the principles outlined in the Declaration of Helsinki, and all applicable federal and local regulations.

Background therapy:

None

Evidence for comparator:

Not applicable

Actual start date of recruitment	06 March 2009
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	Australia: 1992
Worldwide total number of subjects	1992
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)	390
Children (2-11 years)	1384
Adolescents (12-17 years)	218

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

Subject disposition

Recruitment

Recruitment details:

Active Study Initiation Date: 06 March 2009 (First participant, First Visit)

Study Completion Date: 22 February 2010 (Last participant followed up, 180 days after last vaccination)

The study was conducted at seven sites in Australia.

Pre-assignment

Screening details:

2024 participants provided informed consent, 1992 participants were enrolled into the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A

Arm description:

participants aged 6 months to < 3 years

Arm type	Experimental
Investigational medicinal product name	CSL Limited's Influenza Virus Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

The 2009 Southern Hemisphere formulation of CSL's IVV was supplied as a thimerosal-free aqueous suspension in pre-filled syringes. Each 0.25 mL dose contained 7.5 mcg HA antigen for each of the three strains recommended by the World Health Organization for the 2009 Southern Hemisphere influenza season (nominal 22.5 mcg HA antigen per 0.25 mL dose). The dosing regimen (a single vaccination or two vaccinations) was determined by the participant's influenza vaccination history. Participants were administered a single vaccination of CSL's IVV if they had received two doses of influenza vaccine during the 2008 Southern Hemisphere influenza season, or one or more doses of influenza vaccine during an influenza season before 2008. Each vaccination was administered by intramuscular injection into either the anterolateral aspect of the thigh (recommended for participants aged 12 months or younger) or deltoid region of the arm (recommended for participants aged older than 12 months).

Arm title	Cohort B
------------------	----------

Arm description:

participants aged 3 years to < 9 years

Arm type	Experimental
Investigational medicinal product name	CSL Limited's Influenza Virus Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

The 2009 Southern Hemisphere formulation of CSL's IVV was supplied as a thimerosal-free aqueous suspension in pre-filled syringes. Each 0.5 mL dose contained 15 mcg HA antigen for each of the three strains recommended by the World Health Organization for the 2009 Southern Hemisphere influenza season (nominal 45 mcg HA antigen per 0.5 mL dose). The dosing regimen (a single vaccination or two vaccinations) was determined by the participant's influenza vaccination history. Participants were

administered a single vaccination of CSL's IVV if they had received two doses of influenza vaccine during the 2008 Southern Hemisphere influenza season, or one or more doses of influenza vaccine during an influenza season before 2008. Each vaccination was administered by intramuscular injection into the deltoid region of the arm.

Arm title	Cohort C
Arm description: participants aged 9 years to < 18 years	
Arm type	Experimental
Investigational medicinal product name	CSL Limited's Influenza Virus Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

The 2009 Southern Hemisphere formulation of CSL's IVV was supplied as a thimerosal-free aqueous suspension in pre-filled syringes. Each 0.5 mL dose contained 15 mcg HA antigen for each of the three strains recommended by the World Health Organization for the 2009 Southern Hemisphere influenza season (nominal 45 mcg HA antigen per 0.5 mL dose). Participants were administered a single vaccination of CSL's IVV by intramuscular injection into the deltoid region of the arm.

Number of subjects in period 1	Cohort A	Cohort B	Cohort C
Started	710	880	402
Completed	682	859	396
Not completed	28	21	6
Physician decision	2	-	-
Unable to attend study visit	5	2	-
Moved away from study area	1	-	-
Lost to follow-up	9	6	3
Withdrawal by subject	11	13	3

Baseline characteristics

Reporting groups

Reporting group title	Cohort A
Reporting group description: participants aged 6 months to < 3 years	
Reporting group title	Cohort B
Reporting group description: participants aged 3 years to < 9 years	
Reporting group title	Cohort C
Reporting group description: participants aged 9 years to < 18 years	

Reporting group values	Cohort A	Cohort B	Cohort C
Number of subjects	710	880	402
Age categorical Units: Subjects			
Cohort A - 6 months to less than 3 years	710	0	0
Cohort B - 3 to less than 9 years	0	880	0
Cohort C - 9 to less than 18 years	0	0	402
Age continuous Units: years			
arithmetic mean	1.84	5.54	12.64
standard deviation	± 0.74	± 1.66	± 2.48
Gender categorical Units: Subjects			
Female	325	439	202
Male	385	441	200

Reporting group values	Total		
Number of subjects	1992		
Age categorical Units: Subjects			
Cohort A - 6 months to less than 3 years	710		
Cohort B - 3 to less than 9 years	880		
Cohort C - 9 to less than 18 years	402		
Age continuous Units: years			
arithmetic mean	-		
standard deviation	-		
Gender categorical Units: Subjects			
Female	966		
Male	1026		

Subject analysis sets

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

A total of 1992 participants received at least one vaccination with CSL's IVV. Of these, 16 participants did not provide follow-up safety data; therefore, 1976 participants comprised the Safety Set.

Reporting group values	Safety Set		
Number of subjects	1976		
Age categorical Units: Subjects			
Cohort A - 6 months to less than 3 years	710		
Cohort B - 3 to less than 9 years	880		
Cohort C - 9 to less than 18 years	402		
Age continuous Units: years			
arithmetic mean	5.66		
standard deviation	± 4.21		
Gender categorical Units: Subjects			
Female	966		
Male	1026		

End points

End points reporting groups

Reporting group title	Cohort A
Reporting group description:	
participants aged 6 months to < 3 years	
Reporting group title	Cohort B
Reporting group description:	
participants aged 3 years to < 9 years	
Reporting group title	Cohort C
Reporting group description:	
participants aged 9 years to < 18 years	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
A total of 1992 participants received at least one vaccination with CSL's IVV. Of these, 16 participants did not provide follow-up safety data; therefore, 1976 participants comprised the Safety Set.	

Primary: Frequency and Intensity of Solicited Adverse Events after First Vaccination

End point title	Frequency and Intensity of Solicited Adverse Events after First Vaccination ^[1]
End point description:	
Solicited Local Adverse Events: pain, redness, and swelling/induration. Solicited Systemic Adverse Events: fever, headache, myalgia, nausea/vomiting, and diarrhea. Loss of appetite and irritability were also collected in cohort A only. Malaise was also collected in cohorts B and C only.	
End point type	Primary
End point timeframe:	
Collected for 6 days (total 7 days) following vaccination	

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: Summary descriptive statistics of continuous data were presented as number of observations, mean, standard deviation, median, minimum and maximum. For categorical variables, statistical summaries included counts and percentages relative to the appropriate population. A 95% confidence interval was provided for descriptive statistics, as warranted.

End point values	Cohort A	Cohort B	Cohort C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	703	875	398	
Units: Number of subjects				
Any local solicited adverse event	254	512	281	
Any pain	160	463	271	
Grade 3 pain	1	2	1	
Any redness (> 0 mm)	148	189	66	
Grade 3 redness (> 30 mm)	2	18	8	
Any swelling/induration (> 0 mm)	66	137	52	
Grade 3 swelling/induration (> 30 mm)	2	19	12	
Any systemic solicited adverse event	424	346	170	
Any fever (≥99.5°F axillary or ≥100.4 °F oral)	201	171	20	
Grade 3 fever (≥103.1 F°axillary or ≥104 °F oral)	13	7	0	
Any headache	25	136	107	

Grade 3 headache (prevents activities)	1	4	2	
Any myalgia	26	87	80	
Grade 3 myalgia (prevents activities)	3	3	0	
Any nausea/vomiting	79	75	21	
Grade 3 nausea/vomiting (prevents activities)	12	6	1	
Any diarrhea	100	40	21	
Grade 3 diarrhea (prevents activities)	4	2	1	
Any loss of appetite	141	0	0	
Grade 3 loss of appetite (prevents activities)	8	0	0	
Any irritability	295	0	0	
Grade 3 irritability (prevents activities)	24	0	0	
Any malaise	0	179	66	
Grade 3 malaise (prevents activities)	0	14	1	

Statistical analyses

No statistical analyses for this end point

Primary: Duration of Solicited Adverse Events after First Vaccination

End point title	Duration of Solicited Adverse Events after First Vaccination ^[2]
-----------------	---

End point description:

Solicited Local Adverse Events: pain, redness, and swelling/induration. Solicited Systemic Adverse Events: fever, headache, myalgia, nausea/vomiting, and diarrhea. Loss of appetite and irritability were also collected in cohort A only. Malaise was also collected in cohorts B and C only.

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

End point timeframe:

7 days post-vaccination

Notes:

[2] - 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: Summary descriptive statistics of continuous data were presented as number of observations, mean, standard deviation, median, minimum and maximum. For categorical variables, statistical summaries included counts and percentages relative to the appropriate population. A 95% confidence interval was provided for descriptive statistics, as warranted.

End point values	Cohort A	Cohort B	Cohort C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	703	875	398	
Units: Days				
arithmetic mean (standard deviation)				
Any pain	1.83 (± 1.264)	1.89 (± 1.178)	2.02 (± 1.317)	
Any redness (> 0 mm)	2.55 (± 1.93)	2.45 (± 1.713)	2.52 (± 1.867)	
Any swelling / induration (> 0 mm)	3.06 (± 4.011)	2.48 (± 1.688)	2.81 (± 1.854)	
Any fever (≥99.5°F axillary or ≥100.4 °F oral)	1.54 (± 1.164)	1.4 (± 1.114)	1.21 (± 0.415)	
Any headache	2.5 (± 4.492)	1.79 (± 1.373)	1.97 (± 1.851)	
Any myalgia	1.54 (± 1.071)	1.74 (± 1.264)	2.2 (± 3.123)	
Any nausea / vomiting	1.87 (± 2.587)	1.52 (± 1.305)	1.65 (± 1.164)	
Any diarrhea	2.43 (± 3.473)	2 (± 1.593)	2.23 (± 1.771)	
Any loss of appetite	2.53 (± 3.204)	0 (± 0)	0 (± 0)	

Any irritability	2.28 (± 2.503)	0 (± 0)	0 (± 0)	
Any malaise	0 (± 0)	1.89 (± 1.763)	2.56 (± 1.853)	

Statistical analyses

No statistical analyses for this end point

Primary: Frequency and Intensity of Solicited Adverse Events after Second Vaccination

End point title	Frequency and Intensity of Solicited Adverse Events after Second Vaccination ^[3] ^[4]
-----------------	--

End point description:

Solicited Local Adverse Events: pain, redness, and swelling/induration. Solicited Systemic Adverse Events: fever, headache, myalgia, nausea/vomiting, and diarrhea. Loss of appetite and irritability were also collected in cohort A only. Malaise was also collected in cohorts B and C only.

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

End point timeframe:

7 days post-vaccination

Notes:

[3] - 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: Summary descriptive statistics of continuous data were presented as number of observations, mean, standard deviation, median, minimum and maximum. For categorical variables, statistical summaries included counts and percentages relative to the appropriate population. A 95% confidence interval was provided for descriptive statistics, as warranted.

[4] - 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: Participants in Cohort C did not receive a second vaccination.

End point values	Cohort A	Cohort B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	615	634		
Units: Number of Participants				
Any local solicited adverse event	167	312		
Any pain	111	282		
Grade 3 pain	2	2		
Any redness (> 0 mm)	109	109		
Grade 3 redness (> 30 mm)	1	7		
Any swelling / induration (> 0 mm)	64	77		
Grade 3 swelling / induration (> 30 mm)	0	8		
Any systemic solicited adverse event	261	157		
Any fever (≥99.5°F axillary or ≥100.4 °F oral)	110	63		
Grade 3 fever (≥103.1 F°axillary or ≥104 °F oral)	6	2		
Any headache	12	38		
Grade 3 headache (prevent activities)	0	4		
Any myalgia	16	34		
Grade 3 myalgia (prevent activities)	1	3		
Any nausea / vomiting	31	35		

Grade 3 nausea / vomiting (prevent activities)	4	5		
Any diarrhea	52	20		
Grade 3 diarrhea (prevent activities)	3	0		
Any loss of appetite	82	0		
Grade 3 loss of appetite (prevent activities)	4	0		
Any irritability	175	0		
Grade 3 irritability (prevent activities)	7	0		
Any malaise	0	72		
Grade 3 malaise (prevent activities)	0	10		

Statistical analyses

No statistical analyses for this end point

Primary: Duration of Solicited Adverse Events after Second Vaccination

End point title	Duration of Solicited Adverse Events after Second
-----------------	---

End point description:

Solicited Local Adverse Events: pain, redness, and swelling/induration. Solicited Systemic Adverse Events: fever, headache, myalgia, nausea/vomiting, and diarrhea. Loss of appetite and irritability were also collected in cohort A only. Malaise was also collected in cohorts B and C only.

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

End point timeframe:

7 days post-vaccination

Notes:

[5] - 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: Summary descriptive statistics of continuous data were presented as number of observations, mean, standard deviation, median, minimum and maximum. For categorical variables, statistical summaries included counts and percentages relative to the appropriate population. A 95% confidence interval was provided for descriptive statistics, as warranted.

[6] - 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: Participants in Cohort C did not receive a second vaccination.

End point values	Cohort A	Cohort B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	615	634		
Units: Days				
arithmetic mean (standard deviation)				
Any pain	1.76 (± 1.315)	1.68 (± 1.03)		
Any redness (> 0 mm)	2.74 (± 2.478)	2.21 (± 1.316)		
Any swelling / induration (> 0 mm)	3.2 (± 3.301)	2.09 (± 1.696)		
Any fever (≥99.5°F axillary or ≥100.4 °F oral)	1.67 (± 1.148)	1.58 (± 1.117)		
Any headache	1.23 (± 0.439)	1.66 (± 1.311)		
Any myalgia	1.7 (± 1.129)	1.38 (± 0.59)		
Any nausea / vomiting	2.84 (± 4.919)	1.36 (± 0.757)		
Any diarrhea	2.5 (± 2.573)	2 (± 1.612)		
Any loss of appetite	3.02 (± 4.325)	0 (± 0)		
Any irritability	2.42 (± 2.726)	0 (± 0)		

Any malaise	0 ($\pm$ 0)	2.13 ($\pm$ 1.584)		
-------------	--------------	---------------------	--	--

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency and Intensity of Unsolicited Adverse Events (UAEs)

End point title	Frequency and Intensity of Unsolicited Adverse Events (UAEs)
-----------------	--

End point description:

UAE stands for Unsolicited Adverse Event. No statistical analysis provided for frequency and intensity of UAEs

End point type	Secondary
----------------	-----------

End point timeframe:

30 days after each study vaccination

End point values	Cohort A	Cohort B	Cohort C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	703	875	398	
Units: Number of subjects				
Number of participants with at least one UA	531	521	167	
Number of participants reported Grade 1 UAE	115	183	63	
Number of participants reported Grade 2 UAE	300	251	82	
Number of participants reported Grade 3 UAE	116	87	22	

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of Serious Adverse Events (SAEs)

End point title	Frequency of Serious Adverse Events (SAEs)
-----------------	--

End point description:

No statistical analysis provided

End point type	Secondary
----------------	-----------

End point timeframe:

180 days after the last vaccination

End point values	Cohort A	Cohort B	Cohort C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	703	875	398	
Units: Number of participants				
Number of participants with at least one SAE	19	5	2	
Number of participants with related SAE	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of New Onsets of Chronic Illness (NOCIs)

End point title	Frequency of New Onsets of Chronic Illness (NOCIs)
End point description:	
No statistical analysis provided	
End point type	Secondary
End point timeframe:	
180 days after the last study vaccination	

End point values	Cohort A	Cohort B	Cohort C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	703	875	398	
Units: Numbers of participants				
Number of participants with at least one NOCI	10	5	2	
Number of participants with related NOCI	2	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Local and systemic solicited AEs were collected for 7 days after each study vaccination. Unsolicited AEs were collected for 30 days after each study vaccination. SAEs and NOCIs were collected up to 180 days after the last study vaccination.

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	Cohort A
-----------------------	----------

Reporting group description:

participants aged 6 months to < 3 years

Reporting group title	Cohort B
-----------------------	----------

Reporting group description:

participants aged 3 years to < 9 years

Reporting group title	Cohort C
-----------------------	----------

Reporting group description:

participants aged 9 years to less than 18 years

Serious adverse events	Cohort A	Cohort B	Cohort C
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 703 (2.70%)	5 / 875 (0.57%)	2 / 398 (0.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Forearm fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 703 (0.14%)	0 / 875 (0.00%)	0 / 398 (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
Hand fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 703 (0.00%)	1 / 875 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Convulsion alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 703 (0.14%) 0 / 1 0 / 0	0 / 875 (0.00%) 0 / 0 0 / 0	0 / 398 (0.00%) 0 / 0 0 / 0
Febrile convulsion alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 703 (0.14%) 0 / 1 0 / 0	0 / 875 (0.00%) 0 / 0 0 / 0	0 / 398 (0.00%) 0 / 0 0 / 0
Respiratory, thoracic and mediastinal disorders Asthma alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	5 / 703 (0.71%) 0 / 5 0 / 0	0 / 875 (0.00%) 0 / 0 0 / 0	0 / 398 (0.00%) 0 / 0 0 / 0
Pneumonitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 703 (0.14%) 0 / 1 0 / 0	0 / 875 (0.00%) 0 / 0 0 / 0	0 / 398 (0.00%) 0 / 0 0 / 0
Psychiatric disorders Conversion disorder alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 703 (0.00%) 0 / 0 0 / 0	1 / 875 (0.11%) 0 / 1 0 / 0	0 / 398 (0.00%) 0 / 0 0 / 0
Renal and urinary disorders Pelvi-ureteric obstruction alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 703 (0.00%) 0 / 0 0 / 0	1 / 875 (0.11%) 0 / 1 0 / 0	0 / 398 (0.00%) 0 / 0 0 / 0
Infections and infestations Pneumonia			

alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 703 (0.28%)	0 / 875 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 703 (0.14%)	0 / 875 (0.00%)	0 / 398 (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
Croup infectious			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 703 (0.14%)	0 / 875 (0.00%)	0 / 398 (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
Eczema infected			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 703 (0.00%)	1 / 875 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 703 (0.14%)	0 / 875 (0.00%)	0 / 398 (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
Lower respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 703 (0.14%)	0 / 875 (0.00%)	0 / 398 (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
Osteomyelitis			
subjects affected / exposed	1 / 703 (0.14%)	0 / 875 (0.00%)	0 / 398 (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

Pharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 703 (0.00%)	0 / 875 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 703 (0.14%)	0 / 875 (0.00%)	0 / 398 (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
Respiratory tract infection viral			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 703 (0.00%)	1 / 875 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 703 (0.00%)	0 / 875 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 703 (0.14%)	0 / 875 (0.00%)	0 / 398 (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
Viral infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 703 (0.14%)	0 / 875 (0.00%)	0 / 398 (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

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Cohort A	Cohort B	Cohort C
Total subjects affected by non-serious adverse events subjects affected / exposed	531 / 703 (75.53%)	467 / 875 (53.37%)	97 / 398 (24.37%)
Nervous system disorders Headache alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	2 / 703 (0.28%) 3	31 / 875 (3.54%) 38	33 / 398 (8.29%) 37
General disorders and administration site conditions Pyrexia alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	76 / 703 (10.81%) 95	55 / 875 (6.29%) 58	4 / 398 (1.01%) 4
Gastrointestinal disorders Teething alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Vomiting alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	113 / 703 (16.07%) 165 46 / 703 (6.54%) 53	2 / 875 (0.23%) 2 26 / 875 (2.97%) 27	0 / 398 (0.00%) 0 1 / 398 (0.25%) 1
Respiratory, thoracic and mediastinal disorders Cough alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Rhinorrhoea alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	80 / 703 (11.38%) 97 90 / 703 (12.80%) 111	86 / 875 (9.83%) 101 65 / 875 (7.43%) 73	6 / 398 (1.51%) 6 12 / 398 (3.02%) 13
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	36 / 703 (5.12%) 40	10 / 875 (1.14%) 10	1 / 398 (0.25%) 1
Infections and infestations			

Upper respiratory tract infection subjects affected / exposed occurrences (all)	208 / 703 (29.59%) 262	142 / 875 (16.23%) 171	33 / 398 (8.29%) 37
Nasopharyngitis alternative assessment type: Non- systematic subjects affected / exposed occurrences (all)	50 / 703 (7.11%) 59	39 / 875 (4.46%) 46	4 / 398 (1.01%) 4
Respiratory tract infection alternative assessment type: Non- systematic subjects affected / exposed occurrences (all)	37 / 703 (5.26%) 41	11 / 875 (1.26%) 11	3 / 398 (0.75%) 3

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