Clinical trial results:
A phase III open-label study to assess the safety and reactogenicity of GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine when co-administered with GSK Biologicals' Infanrix hexa (DTPa-HBV-IPV/Hib) vaccine as a 3-dose primary immunization course at 2, 3 and 4 months of age in infants in Vietnam.

Summary

EudraCT number	2012-000162-38
Trial protocol	Outside EU/EEA
Global end of trial date	26 July 2011

Results information

Result version number	v2 (current)
This version publication date	05 March 2023
First version publication date	05 July 2015
Version creation reason	• Correction of full data set Correction of full data set and alignment between registries.

Trial information

Trial identification

Sponsor protocol code	113151

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01153841
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut, 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 October 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 July 2011
Global end of trial reached?	Yes
Global end of trial date	26 July 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and reactogenicity of GSK Biologicals' 10-valent pneumococcal conjugate vaccine (Synflorix - 10Pn) vaccine when co-administered with Infanrix hexa (DTPa-HBV-IPV/Hib) vaccine as a 3-dose primary vaccination course at 2, 3 and 4 months of age, in terms of grade 3 solicited and unsolicited adverse events (AEs).

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 February 2011
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	Vietnam: 300
Worldwide total number of subjects	300
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)	300
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

300 subjects were enrolled in this study. 2 subjects among the 101 subjects in the Infanrix Hexa Group were not vaccinated due to consent withdrawal.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Synflorix+Infanrix hexa Group

Arm description:

Healthy male or female subjects who received the Synflorix vaccine, intramuscularly in the right thigh, co-administered along with the Infanrix hexa vaccine, intramuscularly in the left thigh, according to a 3-dose schedule at 2, 3 and 4 months of age.

Arm type	Experimental
Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	GSK1024850A, 10Pn
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered, according to a 3 dose schedule at 2, 3 and 4 months of age, in the right thigh.

Investigational medicinal product name	Infanrix hexa™
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered by intramuscular injection in the left thigh, according to a 3 dose schedule at 2, 3 and 4 months of age.

Arm title	Infanrix Hexa Group

Arm description:

Healthy male or female subjects who received the Infanrix hexa vaccine alone, administered intramuscularly in the left thigh, according to a 3-dose schedule at 2, 3 and 4 months of age.

Arm type	Active comparator
Investigational medicinal product name	Infanrix hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered by intramuscular injection in the left thigh, according to a 3 dose schedule at 2, 3 and 4 months of age.

Number of subjects in period 1[1]	Synflorix+Infanrix hexa Group	Infanrix Hexa Group
Started	199	99
Completed	193	99
Not completed	6	0
Consent withdrawn by subject	1	-
Adverse event, non-fatal	1	-
Protocol deviation	2	-
Lost to follow-up	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: 300 subjects were enrolled in this study. 2 subjects among the 101 subjects in the Infanrix Hexa Group were not vaccinated due to consent withdrawal.

Baseline characteristics

Reporting groups	
Reporting group title	Synflorix+Infanrix hexa Group
Reporting group description:	
Healthy male or female subjects who received the Synflorix vaccine, intramuscularly in the right thigh, co-administered along with the Infanrix hexa vaccine, intramuscularly in the left thigh, according to a 3-dose schedule at 2, 3 and 4 months of age.	
Reporting group title	Infanrix Hexa Group
Reporting group description:	
Healthy male or female subjects who received the Infanrix hexa vaccine alone, administered intramuscularly in the left thigh, according to a 3-dose schedule at 2, 3 and 4 months of age.	

Reporting group values	Synflorix+Infanrix hexa Group	Infanrix Hexa Group	Total
Number of subjects	199	99	298
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	199	99	298
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: weeks			
arithmetic mean	8.8	8.7	
standard deviation	± 1.24	± 1.11	-
Gender categorical Units: Subjects			
Female	93	37	130
Male	106	62	168

End points

End points reporting groups

Reporting group title	Synflorix+Infanrix hexa Group

Reporting group description:

Healthy male or female subjects who received the Synflorix vaccine, intramuscularly in the right thigh, co-administered along with the Infanrix hexa vaccine, intramuscularly in the left thigh, according to a 3-dose schedule at 2, 3 and 4 months of age.

Reporting group title	Infanrix Hexa Group

Reporting group description:

Healthy male or female subjects who received the Infanrix hexa vaccine alone, administered intramuscularly in the left thigh, according to a 3-dose schedule at 2, 3 and 4 months of age.

Primary: Number of subjects with Grade 3 symptoms (solicited and unsolicited)

End point title	Number of subjects with Grade 3 symptoms (solicited and unsolicited)[1]

End point description:

The incidence and nature of Grade 3 symptoms (solicited and unsolicited) reported during the 31-day post-vaccination period following each dose and across doses are presented.
The analysis was performed on the Total Vaccinated cohort, which included all vaccinated subjects with at least one vaccine administration documented and with the symptom sheet filled in.

End point type	Primary

End point timeframe:

Within the 31-day (Days 0-30) after each dose and across doses

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Synflorix+Infanrix hexa Group	Infanrix Hexa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	99		
Units: Subjects				
Any symptom Dose 1 [N=197,99]	24	3		
Any symptom Dose 2 [N=193,99]	18	3		
Any symptom Dose 3 [N=193,99]	6	3		
Any symptom Across doses [N=197,99]	32	9		
General symptoms Dose 1 [N=197,99]	5	1		
General symptoms Dose 2 [N=193,99]	7	1		
General symptoms Dose 3 [N=193,99]	1	1		
General symptoms Across doses [N=197,99]	10	3		
Local symptoms Dose 1 [N=197,99]	23	2		
Local symptoms Dose 2 [N=193,99]	15	2		
Local symptoms Dose 3 [N=193,99]	5	2		
Local symptoms Dose Across doses [N=197,99]	28	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptoms

End point title	Number of subjects reporting any and grade 3 solicited local symptoms

End point description:

Solicited local symptoms assessed include pain, redness and swelling. Grade 3 pain was defined as crying when limb was moved/spontaneously painful. Grade 3 swelling/redness was defined as swelling/redness greater than (>) 30 millimeters (mm). "Any" is defined as incidence of the specified symptom regardless of intensity.
The analysis was performed on the Total Vaccinated cohort, which included all vaccinated subjects with at least one vaccine administration documented and with the symptom sheet filled in.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose

End point values	Synflorix+Infanrix hexa Group	Infanrix Hexa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	99		
Units: Subjects				
Any Pain Dose 1 [N=197;99]	116	34		
Grade 3 Pain Dose 1 [N=197;99]	22	1		
Any Redness Dose 1 [N=197;99]	48	13		
Grade 3 Redness Dose 1 [N=197;99]	3	0		
Any Swelling Dose 1 [N=197;99]	47	10		
Grade 3 Swelling Dose 1 [N=197;99]	3	1		
Any Pain Dose 2 [N=193;99]	101	31		
Grade 3 Pain Dose 2 [N=193;99]	12	2		
Any Redness Dose 2 [N=193;99]	49	19		
Grade 3 Redness Dose 2 [N=193;99]	1	0		
Any Swelling Dose 2 [N=193;99]	44	12		
Grade 3 Swelling Dose 2 [N=193;99]	2	0		
Any Pain Dose 3 [N=193;99]	68	27		
Grade 3 Pain Dose 3 [N=193;99]	4	0		
Any Redness Dose 3 [N=193;99]	38	12		
Grade 3 Redness Dose 3 [N=193;99]	1	1		
Any Swelling Dose 3 [N=193;99]	29	12		
Grade 3 Swelling Dose 3 [N=193;99]	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general symptoms

End point title	Number of subjects reporting any, grade 3 and related solicited general symptoms

End point description:

Solicited general symptoms assessed include drowsiness, fever (defined as axillary temperature greater than or equal to [≥] 37.5°C), irritability, and loss of appetite. Grade 3 drowsiness was defined as drowsiness which prevented normal everyday activities. Grade 3 fever was defined as fever (axillary temperature) greater than (>) 39.5 degree Celsius (°C). Grade 3 irritability was defined as crying that could not be comforted/preventing normal activity. Grade 3 loss of appetite was defined as the subject not eating at all. "Any" is defined as incidence of the specified symptom regardless of intensity or relationship to study vaccination.
The analysis was performed on the Total Vaccinated cohort, which included all vaccinated subjects with at least one vaccine administration documented and with the symptom sheet filled in.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose

End point values	Synflorix+Infanrix hexa Group	Infanrix Hexa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	99		
Units: Subjects				
Any Drowsiness Dose 1 [N=197;99]	75	19		
Grade 3 Drowsiness Dose 1 [N=197;99]	3	0		
Related Drowsiness Dose 1 [N=197;99]	60	15		
Any Fever Dose 1 [N=197;99]	147	36		
Grade 3 Fever Dose 1 [N=197;99]	0	0		
Related Fever Dose 1 [N=197;99]	142	34		
Any Irritability Dose 1 [N=197;99]	155	53		
Grade 3 Irritability Dose 1 [N=197;99]	4	1		
Related Irritability Dose 1 [N=197;99]	146	51		
Any Loss of appetite Dose 1 [N=197;99]	109	40		
Grade 3 Loss of appetite Dose 1 [N=197;99]	0	0		
Related Loss of appetite Dose 1 [N=197;99]	86	31		
Any Drowsiness Dose 2 [N=193;99]	53	10		
Grade 3 Drowsiness Dose 2 [N=193;99]	0	0		
Related Drowsiness Dose 2 [N=193;99]	52	8		

Any Fever Dose 2 [N=193;99]	108	16		
Grade 3 Fever Dose 2 [N=193;99]	0	0		
Related Fever Dose 2 [N=193;99]	105	15		
Any Irritability Dose 2 [N=193;99]	112	36		
Grade 3 Irritability Dose 2 [N=193;99]	6	0		
Related Irritability Dose 2 [N=193;99]	110	32		
Any Loss of appetite Dose 2 [N=193;99]	94	25		
Grade 3 Loss of appetite Dose 2 [N=193;99]	0	0		
Related Loss of appetite Dose 2 [N=193;99]	90	23		
Any Drowsiness Dose 3 [N=193;99]	25	5		
Grade 3 Drowsiness Dose 3 [N=193;99]	0	0		
Related Drowsiness Dose 3 [N=193;99]	21	4		
Any Fever Dose 3 [N=193;99]	63	12		
Grade 3 Fever Dose 3 [N=193;99]	0	1		
Related Fever Dose 3 [N=193;99]	60	12		
Any Irritability Dose 3 [N=193;99]	71	31		
Grade 3 Irritability Dose 3 [N=193;99]	1	0		
Related Irritability Dose 3 [N=193;99]	69	29		
Any Loss of appetite Dose 3 [N=193;99]	67	21		
Grade 3 Loss of appetite Dose 3 [N=193;99]	0	0		
Related Loss of appetite Dose 3[N=193;99]	60	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs)

End point title	Number of subjects with unsolicited adverse events (AEs)

End point description:

An unsolicited AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. “Any” is defined as incidence of an unsolicited AE regardless of intensity or relationship to study vaccination.
The analysis was performed on the Total Vaccinated cohort, which included all vaccinated subjects with at least one vaccine administration documented.

End point type	Secondary

End point timeframe:

During the 31-day (Days 0-30) follow-up period after each dose

End point values	Synflorix+Infanrix hexa Group	Infanrix Hexa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	99		
Units: Subjects				
Any AE(s)	57	37		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs)

End point title	Number of subjects with serious adverse events (SAEs)

End point description:

SAEs assessed include medical occurrences that result in death, are life-threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.
The analysis was performed on the Total Vaccinated cohort, which included all vaccinated subjects with at least one vaccine administration documented.

End point type	Secondary

End point timeframe:

After the first vaccination up to study end (From Month 0 to Month 3)

End point values	Synflorix+Infanrix hexa Group	Infanrix Hexa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	99		
Units: Subjects				
Any SAE(s)	9	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms: during the 4-day (Day 0 - Day 3) post-vaccination period; Unsolicited AEs: during the 31-day (Day 0 - Day 30) post-vaccination period; SAEs: after the first vaccination up to study end (from Month 0 to Month 3).

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	Synflorix+Infanrix hexa Group

Reporting group description: -

Reporting group title	Infanrix hexa Group

Reporting group description: -

Serious adverse events	Synflorix+Infanrix hexa Group	Infanrix hexa Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 199 (4.52%)	6 / 99 (6.06%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Vascular disorders			
Kawasaki’s disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Convulsion			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 199 (0.50%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Autoimmune thrombocytopenia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 199 (0.50%)	2 / 99 (2.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 199 (0.50%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
alternative assessment type: Non-systematic			

subjects affected / exposed	2 / 199 (1.01%)	3 / 99 (3.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superinfection fungal			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 199 (0.50%)	2 / 99 (2.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 199 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 199 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 199 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Synflorix+Infanrix hexa Group	Infanrix hexa Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	195 / 199 (97.99%)	91 / 99 (91.92%)	
General disorders and administration site conditions			
Pain			
subjects affected / exposed[1]	137 / 197 (69.54%)	45 / 99 (45.45%)	
occurrences (all)	137	45	
Redness			
subjects affected / exposed[2]	90 / 197 (45.69%)	29 / 99 (29.29%)	
occurrences (all)	90	29	
Swelling			
subjects affected / exposed[3]	80 / 197 (40.61%)	21 / 99 (21.21%)	
occurrences (all)	80	21	
Drowsiness			
subjects affected / exposed[4]	95 / 197 (48.22%)	26 / 99 (26.26%)	
occurrences (all)	95	26	
Fever (Axillary)			
subjects affected / exposed[5]	172 / 197 (87.31%)	50 / 99 (50.51%)	
occurrences (all)	172	50	
Irritability			
subjects affected / exposed	169 / 199 (84.92%)	63 / 99 (63.64%)	
occurrences (all)	169	63	
Loss of appetite			
subjects affected / exposed[6]	141 / 197 (71.57%)	50 / 99 (50.51%)	
occurrences (all)	141	50	
Respiratory, thoracic and mediastinal disorders			
Wheezing			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 199 (0.50%)	5 / 99 (5.05%)	
occurrences (all)	1	5	
Infections and infestations			
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	20 / 199 (10.05%)	8 / 99 (8.08%)	
occurrences (all)	20	8	
Bronchiolitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	9 / 199 (4.52%)	9 / 99 (9.09%)	
occurrences (all)	9	9	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this phase was performed solely on subjects with their symptom sheets completed.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this phase was performed solely on subjects with their symptom sheets completed.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this phase was performed solely on subjects with their symptom sheets completed.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this phase was performed solely on subjects with their symptom sheets completed.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this phase was performed solely on subjects with their symptom sheets completed.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this phase was performed solely on subjects with their symptom sheets completed.

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