Clinical trial results:
A phase III, open, multicentre, extension study to assess the immune response following administration of an additional dose of GSK Biologicals' 10-valent conjugate pneumococcal vaccine or Prevenar™ at approximately 4 years of age in children previously vaccinated with three primary doses of a pneumococcal conjugate vaccine in study 10PN-PD-DIT-003 (105554) and a booster dose of 23-valent pneumococcal plain polysaccharide vaccine in study 10PN-PD-DIT-008 BST: 003 (106623).

Summary

EudraCT number	2008-007605-37
Trial protocol	DE
Global end of trial date	05 October 2009

Results information

Result version number	v1
This version publication date	05 April 2016
First version publication date	04 June 2015

Trial information

Trial identification

Sponsor protocol code	112807

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00907777
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, B-1330, Belgium, Belgium,
Public contact	GlaxoSmithKline Biologicals, Clinical Trials Call Center, GlaxoSmithKline Biologicals, Clinical Trials Call Center, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, Clinical Trials Call Center, 044 2089-904466, 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?	Yes
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	26 March 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 October 2009
Global end of trial reached?	Yes
Global end of trial date	05 October 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immune response following administration of an additional dose of GSK Biologicals' 10-valent conjugate pneumococcal vaccine (10Pn-PD-DiT) at approximately 4 years of age in children previously vaccinated with 3 doses of 10Pn-PD-DiT vaccine followed by a single dose of 23vPS(Pneumovax 23) vaccine.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 June 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 52
Worldwide total number of subjects	52
EEA total number of subjects	52

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)	52
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:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms

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	Prev group

Arm description:

Subjects receiving Prevenar™ vaccine (Pfizer's 7-valent pneumococcal conjugate vaccine) at approximately 4 years of age in children previously
vaccinated with three primary doses of a pneumococcal conjugate vaccine in study 2005-003299-40 (10PN-PD-DIT-003 [105554]) and a booster dose of 23-valent pneumococcal plain polysaccharide vaccine in study 2006-000560-93 (10PN-PD-DIT-008 BST: 003 [106623])

Arm type	Active comparator
Investigational medicinal product name	Prevenar™
Investigational medicinal product code	
Other name	Pfizer's 7-valent pneumococcal conjugate vaccine, 7Pn
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccine was administered intramuscularly in the deltoid

Arm title	Pn group

Arm description:

Subjects receiving GSK 1024850A vaccine (10-valent pneumococcal polysaccharide and non typeable Haemophilus influenzae protein D conjugate vaccine) at approximately 4 years of age in children previously vaccinated with three primary doses of a pneumococcal conjugate
vaccine in study 2005-003299-40 (10PN-PD-DIT-003 [105554]) and a booster dose of 23-valent pneumococcal plain polysaccharide vaccine in study 2006-000560-93(10PN-PD-DIT-008 BST: 003 [106623])

Arm type	Experimental
Investigational medicinal product name	10-valent Streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn, 10Pn-PD-DiT, GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine, Synflorix™, GSK1024850A
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccine was administered intramuscularly in the deltoid

Number of subjects in period 1	Prev group	Pn group
Started	25	27
Completed	25	26
Not completed	0	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Prev group
Reporting group description:	
Subjects receiving Prevenar™ vaccine (Pfizer's 7-valent pneumococcal conjugate vaccine) at approximately 4 years of age in children previously vaccinated with three primary doses of a pneumococcal conjugate vaccine in study 2005-003299-40 (10PN-PD-DIT-003 [105554]) and a booster dose of 23-valent pneumococcal plain polysaccharide vaccine in study 2006-000560-93 (10PN-PD-DIT-008 BST: 003 [106623])	
Reporting group title	Pn group
Reporting group description:	
Subjects receiving GSK 1024850A vaccine (10-valent pneumococcal polysaccharide and non typeable Haemophilus influenzae protein D conjugate vaccine) at approximately 4 years of age in children previously vaccinated with three primary doses of a pneumococcal conjugate vaccine in study 2005-003299-40 (10PN-PD-DIT-003 [105554]) and a booster dose of 23-valent pneumococcal plain polysaccharide vaccine in study 2006-000560-93(10PN-PD-DIT-008 BST: 003 [106623])	

Reporting group values	Prev group	Pn group	Total
Number of subjects	25	27	52
Age categorical 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)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: months			
arithmetic mean	46.6	46.7	
standard deviation	± 0.91	± 0.72	-
Gender categorical Units: Subjects			
Female	9	17	26
Male	16	10	26

End points

End points reporting groups

Reporting group title	Prev group
Reporting group description:	
Subjects receiving Prevenar™ vaccine (Pfizer's 7-valent pneumococcal conjugate vaccine) at approximately 4 years of age in children previously vaccinated with three primary doses of a pneumococcal conjugate vaccine in study 2005-003299-40 (10PN-PD-DIT-003 [105554]) and a booster dose of 23-valent pneumococcal plain polysaccharide vaccine in study 2006-000560-93 (10PN-PD-DIT-008 BST: 003 [106623])	
Reporting group title	Pn group
Reporting group description:	
Subjects receiving GSK 1024850A vaccine (10-valent pneumococcal polysaccharide and non typeable Haemophilus influenzae protein D conjugate vaccine) at approximately 4 years of age in children previously vaccinated with three primary doses of a pneumococcal conjugate vaccine in study 2005-003299-40 (10PN-PD-DIT-003 [105554]) and a booster dose of 23-valent pneumococcal plain polysaccharide vaccine in study 2006-000560-93(10PN-PD-DIT-008 BST: 003 [106623])	

Primary: Vaccine pneumococcal serotype antibody concentrations

End point title	Vaccine pneumococcal serotype antibody concentrations[1]
End point description:	
Anti-pneumococcal antibody concentration cut-off value assessed >= 0.05 microgram per milliliter (µg/mL). The vaccine pneumococcal serotypes assessed include 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F.	
End point type	Primary
End point timeframe:	
Before (Pre) and one month after (Post) the additional administration	

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	Prev group	Pn group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	26		
Units: µg/mL				
geometric mean (confidence interval 95%)				
ANTI-1 Pre (21,24)	0.14 (0.09 to 0.23)	0.38 (0.25 to 0.56)		
ANTI-1 Post (24,26)	0.16 (0.1 to 0.25)	1.35 (1.05 to 1.73)		
ANTI-4 Pre (21,24)	0.27 (0.15 to 0.5)	0.12 (0.08 to 0.19)		
ANTI-4 Post (24,26)	4.3 (3.38 to 5.48)	6.76 (4.91 to 9.3)		
ANTI-5 Pre (21,24)	0.11 (0.08 to 0.16)	0.5 (0.34 to 0.75)		
ANTI-5 Post (24,26)	0.15 (0.1 to 0.22)	1.78 (1.34 to 2.37)		
ANTI-6B Pre (21,23)	0.65 (0.38 to 1.12)	0.48 (0.26 to 0.88)		

ANTI-6B Post (24,26)	7.46 (4.61 to 12.08)	1.68 (1.1 to 2.56)		
ANTI-7F Pre (21,24)	0.18 (0.1 to 0.32)	0.39 (0.26 to 0.59)		
ANTI-7F Post (24,26)	0.19 (0.11 to 0.32)	2.53 (1.83 to 3.51)		
ANTI-9V Pre (21,24)	0.48 (0.27 to 0.86)	0.44 (0.29 to 0.65)		
ANTI-9V Post (24,26)	6.88 (4.98 to 9.51)	2.13 (1.54 to 2.94)		
ANTI-14 Pre (21,24)	1.5 (0.82 to 2.74)	1.98 (1.14 to 3.42)		
ANTI-14 Post (24,26)	25.82 (14.65 to 45.5)	9.71 (5.61 to 16.82)		
ANTI-18C Pre (21,24)	0.34 (0.2 to 0.58)	0.48 (0.26 to 0.9)		
ANTI-18C Post (24,26)	4.23 (2.94 to 6.08)	6.4 (4.61 to 8.87)		
ANTI-19F Pre (21,23)	2.02 (1.29 to 3.16)	2.37 (1.41 to 3.98)		
ANTI-19F Post (24,26)	5.68 (3.82 to 8.45)	15.61 (11.51 to 21.18)		
ANTI-23F Pre (21,24)	0.33 (0.2 to 0.53)	0.23 (0.12 to 0.43)		
ANTI-23F Post (24,26)	5.82 (3.77 to 8.97)	1.27 (0.9 to 1.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity against vaccine pneumococcal serotypes

End point title	Opsonophagocytic activity against vaccine pneumococcal serotypes

End point description:

Opsonophagocytic activity cut-off value assessed >= 8. The vaccine pneumococcal serotypes assessed include 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F.

End point type	Secondary

End point timeframe:

Before (pre) and one month after (post) the additional administration

End point values	Prev group	Pn group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	26		
Units: titer				
geometric mean (confidence interval 95%)				
OPSONO-1 Pre (22,25)	4 (4 to 4)	5.8 (3.6 to 9.4)		
OPSONO-1 Post (24,25)	5.5 (3.4 to 9.1)	49.3 (25.5 to 95.2)		
OPSONO-4 Pre (21,23)	20.7 (6.4 to 67.5)	12.3 (4.5 to 33.9)		

OPSONO-4 Post (24,26)	4814 (3380.8 to 6854.6)	4380.7 (3020.5 to 6353.4)		
OPSONO-5 Pre (23,25)	4.2 (3.8 to 4.6)	7.5 (4.5 to 12.5)		
OPSONO-5 Post (24,25)	4.4 (3.8 to 5.1)	50.6 (30.8 to 83)		
OPSONO-6B Pre (22,24)	188.2 (55.5 to 638)	66.3 (19.7 to 222.7)		
OPSONO-6B Post (24,26)	6734.3 (3873.2 to 11708.7)	1424.5 (775 to 2618.4)		
OPSONO-7F Pre (22,24)	1202.9 (809 to 1788.8)	1498.9 (1097.8 to 2046.6)		
OPSONO-7F Post (24,26)	1304.2 (880.7 to 1931.4)	4657.1 (3321.2 to 6530.3)		
OPSONO-9V Pre (22,23)	612.9 (458.6 to 819.3)	442 (224.5 to 870.3)		
OPSONO-9V Post (23,26)	5829.4 (3909.1 to 8693.2)	2843.5 (2016 to 4010.6)		
OPSONO-14 Pre (21,25)	149.7 (65.2 to 343.5)	330 (186.5 to 584)		
OPSONO-14 Post (24,26)	5400.8 (3491.3 to 8354.8)	2812.4 (1734.3 to 4560.7)		
OPSONO-18C Pre (21,24)	16.1 (5.3 to 49.2)	23.7 (7.5 to 74.2)		
OPSONO-18C Post (24,25)	1615.2 (782 to 3336.1)	2806.6 (1408.8 to 5591.2)		
OPSONO-19F Pre (22,25)	26.1 (14.8 to 46.1)	35.8 (18.6 to 68.8)		
OPSONO-19F Post (24,25)	241.6 (133.6 to 436.7)	837.3 (559.5 to 1253.2)		
OPSONO-23F Pre (21,25)	1430.2 (542.5 to 3770.6)	1383.2 (630.2 to 3036)		
OPSONO-23F Post (24,26)	23977.2 (14185.3 to 40528.2)	4865.1 (3977 to 5951.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cross-reactive pneumococcal serotype antibody concentrations

End point title	Cross-reactive pneumococcal serotype antibody concentrations

End point description:

Anti-pneumococcal antibody concentration cut-off value assessed >= 0.05 microgram per milliliter (µg/mL). The cross-reactive pneumococcal serotypes assessed include 6A and 19A.

End point type	Secondary

End point timeframe:

Before (pre) and one month after (post) the additional administration

End point values	Prev group	Pn group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	26		
Units: µg/mL				
geometric mean (confidence interval 95%)				
ANTI-6A Pre (21,24)	0.22 (0.13 to 0.37)	0.19 (0.12 to 0.32)		
ANTI-6A Post (24,26)	1.78 (0.88 to 3.59)	0.47 (0.29 to 0.75)		
ANTI-19A Pre (21,24)	0.39 (0.2 to 0.78)	0.29 (0.17 to 0.5)		
ANTI-19A Post (24,26)	0.8 (0.44 to 1.44)	1.24 (0.79 to 1.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity against cross-reactive pneumococcal serotypes

End point title	Opsonophagocytic activity against cross-reactive pneumococcal serotypes

End point description:

Opsonophagocytic activity cut-off value assessed >= 8. The cross-reactive pneumococcal serotypes assessed include 6A and 19A.

End point type	Secondary

End point timeframe:

Before (pre) and one month after (post) the additional administration

End point values	Prev group	Pn group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: Titer				
geometric mean (confidence interval 95%)				
OPSONO-6A Pre (20,22)	106.9 (44.7 to 255.7)	117.7 (43.6 to 318.3)		
OPSONO-6A Post (24,22)	2320.4 (1180.2 to 4562.5)	966.2 (634.8 to 1470.6)		
OPSONO-19A Pre (23,23)	10.4 (4.9 to 22.1)	19.6 (6.6 to 58.8)		
OPSONO-19A Post (24,24)	101.3 (42.7 to 240.7)	153.9 (67.7 to 349.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-protein D antibody concentrations

End point title	Anti-protein D antibody concentrations

End point description:

Anti-protein D antibody cut-off value (>=100 EL.U/mL) was assessed by Enzyme-Linked Immuno Sorbent Assay (ELISA) unit per milliliter (EL.U/mL).

End point type	Secondary

End point timeframe:

Before (pre) and one month after (post) the additional administration

End point values	Prev group	Pn group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	26		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
ANTI-PD Pre (21,23)	104.1 (76.8 to 140.9)	173.1 (113.5 to 263.9)		
ANTI-PD Post (24,26)	85.9 (64.1 to 115)	1135.6 (709 to 1819)		

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 general 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 larger (>) 30 millimeters (mm). "Any" is defined as incidence of the specified symptom regardless of intensity.

End point type	Secondary

End point timeframe:

During the 8-day (Days 0-7) post-additional dose

End point values	Prev group	Pn group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: Subjects				
Pain (Any)	11	16		
Pain (Grade 3)	0	2		
Redness (Any)	13	14		
Redness (Grade 3)	7	3		
Swelling (Any)	7	9		
Swelling (Grade 3)	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any , Grade 3 and related solicited general symptoms

End point title	Number of subjects with any , Grade 3 and related solicited general symptoms

End point description:

Solicited general symptoms assessed include drowsiness, fever (defined as rectal temperature ≥ 38.0°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 (rectal temperature) above (>) 40.0 degree Celsius (°C). Grade 3 irritability was defined as crying that could not be comforted/preventing normal everyday activities. 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

End point type	Secondary

End point timeframe:

During the 8-day (Days 0-7) post-additional dose

End point values	Prev group	Pn group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: Subjects				
Drowsiness (Any)	4	12		
Drowsiness (Grade 3)	0	1		
Drowsiness (Related)	0	8		
Fever (Any)	1	8		
Fever (Grade 3)	0	0		
Fever (Related)	0	6		
Irritability (Any)	5	9		
Irritability (Grade 3)	0	1		
Irritability (Related)	2	7		
Loss of appetite (Any)	3	12		

Loss of appetite (Grade 3)	0	2		
Loss of appetite (Related)	1	7		

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 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 an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination.

End point type	Secondary

End point timeframe:

Within 31 days (Day 0-30) post-additional vaccination

End point values	Prev group	Pn group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Subjects				
Any AEs	8	6		

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:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or may evolve into one of the outcomes listed above.

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Prev group	Pn group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Subjects				
Subject(s) with SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events: entire study period;
Solicited local and general symptoms: Within 8 days after the additional vaccination;
Unsolicited symptoms: Within 31 days after the additional vaccination

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	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	Pn group

Reporting group description:

Subjects receiving GSK 1024850A vaccine (10-valent pneumococcal polysaccharide and non typeable Haemophilus influenzae protein D conjugate vaccine) at approximately 4 years of age in children previously vaccinated with three primary doses of a pneumococcal conjugate vaccine in study 2005-003299-40 (10PN-PD-DIT-003 [105554]) and a booster dose of 23-valent pneumococcal plain polysaccharide vaccine in study 2006-000560-93 (10PN-PD-DIT-008 BST: 003 [106623])

Reporting group title	Prev group

Reporting group description:

Subjects receiving Prevenar™ vaccine (Pfizer's 7-valent pneumococcal conjugate vaccine) at approximately 4 years of age in children previously vaccinated with three primary doses of a pneumococcal conjugate vaccine in study 2005-003299-40 (10PN-PD-DIT-003 [105554]) and a booster dose of 23-valent pneumococcal plain polysaccharide vaccine in study 2006-000560-93 (10PN-PD-DIT-008 BST: 003 [106623])

Serious adverse events	Pn group	Prev group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)	0 / 25 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Pn group	Prev group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 27 (59.26%)	13 / 25 (52.00%)	
General disorders and administration site conditions			

Pain			
subjects affected / exposed[1]	16 / 26 (61.54%)	11 / 25 (44.00%)	
occurrences (all)	16	11	
Redness			
subjects affected / exposed[2]	14 / 26 (53.85%)	13 / 25 (52.00%)	
occurrences (all)	14	13	
Swelling			
subjects affected / exposed[3]	9 / 26 (34.62%)	7 / 25 (28.00%)	
occurrences (all)	9	7	
Drowsiness			
subjects affected / exposed[4]	12 / 26 (46.15%)	4 / 25 (16.00%)	
occurrences (all)	12	4	
Fever (>38.0°C)			
subjects affected / exposed[5]	8 / 26 (30.77%)	1 / 25 (4.00%)	
occurrences (all)	8	1	
Irritability			
subjects affected / exposed[6]	9 / 26 (34.62%)	5 / 25 (20.00%)	
occurrences (all)	9	5	
Loss of appetite			
subjects affected / exposed[7]	12 / 26 (46.15%)	3 / 25 (12.00%)	
occurrences (all)	12	3	

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: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

[7] - 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: The analysis of the solicited symptom included only subjects with documented data.

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None reported

Notes: