



Clinical trial results:

A phase II, observer-blind follow-up study with two groups to assess the reactogenicity and immunogenicity of GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine (GSK1024850A), when either given as a booster dose (at 20-23 months of age) in children previously primed with three doses of the study vaccine, or when given as a two-dose catch-up immunization (at 18-21 and 20-23 months of age) in unprimed children, all previously enrolled in the 10PN-PD-DIT-005 primary vaccination study.

Summary

EudraCT number	2015-001449-93
Trial protocol	Outside EU/EEA
Global end of trial date	28 August 2008

Results information

Result version number	v2 (current)
This version publication date	18 April 2021
First version publication date	29 July 2015
Version creation reason	• Correction of full data set - Minor corrections in safety section.

Trial information

Trial identification

Sponsor protocol code	110031
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00513409
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, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 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	Yes

1901/2006 apply to this trial?

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 February 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 August 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the reactogenicity of study vaccines in terms of the occurrence of adverse events with intensity grade 3

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	22 August 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Chile: 163
Worldwide total number of subjects	163
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)	163

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:

The study included an active phase, from Month 0 to Month 3, aka one month post Dose 2 of vaccine, followed by an extended safety follow-up phase of 5 months.

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 Study Period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Single blind ^[1]
Roles blinded	Investigator, Data analyst ^[2]

Blinding implementation details:

This study was conducted in an observer-blind fashion. A different person than that who performed immunogenicity & safety assessments administered study vaccines. The person responsible for preparing and administering vaccine did not have access to safety & reactogenicity information of the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Synflorix Booster Group

Arm description:

Subjects in this group had been previously primed with Synflorix™ and Infanrix™ hexa as part of the 10PN-PD-DIT-005 primary vaccination study, received in this study one dose of Havrix™ co-administered with one dose of Infanrix™ hexa at Month 0 (Dose 1) and one dose of Synflorix™ at Month 2 (Dose 2).

Arm type	Experimental
Investigational medicinal product name	10-valent pneumococcal conjugate vaccine
Investigational medicinal product code	10Pn-PD-DiT
Other name	10Pn, Synforix
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One intramuscular injection Intramuscular injection, administered in the right thigh or deltoid region.

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

Dosage and administration details:

One intramuscular injection administered in the left thigh or deltoid region

Investigational medicinal product name	Havrix 720 Junior
Investigational medicinal product code	HAV 720
Other name	HAV
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One intramuscular injection administered in the right thigh or deltoid region

Arm title	Synflorix Catch-up Group
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Arm description:

Subjects in this group were subjects previously primed with Havrix™ and Infanrix™ hexa co-administered with Infanrix™ hexa as part of 10PN-PD-DIT-005 primary vaccination study and who received in this study a catch-up dose of Synflorix™ co-administered with Infanrix™ hexa at Month 0 (Dose 1) and one booster dose of Synflorix™ at Month 2 (Dose 2).

Arm type	Experimental
Investigational medicinal product name	10-valent pneumococcal conjugate vaccine
Investigational medicinal product code	10Pn-PD-DiT
Other name	10Pn, Synforix
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two intramuscular injections administered in the right thigh or deltoid region

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

Dosage and administration details:

One intramuscular injection administered in the left thigh or deltoid region

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.

Justification: This study was conducted in an observer-blind fashion. A different person than that who performed immunogenicity & safety assessments administered study vaccines. The person responsible for preparing and administering vaccine did not have access to safety & reactogenicity information of the study.

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: This study was conducted in an observer-blind fashion. A different person than that who performed immunogenicity & safety assessments administered study vaccines. The person responsible for preparing and administering vaccine did not have access to safety & reactogenicity information of the study.

Number of subjects in period 1	Synflorix Booster Group	Synflorix Catch-up Group
Started	84	79
Completed	82	73
Not completed	2	6
Consent withdrawn by subject	-	2
Physician Decision	1	-
Adverse event, non-fatal	-	1
Month 3 (Visit 3) not done	-	2
Lost to follow-up	-	1
Visit 3 not done	1	-

Baseline characteristics

Reporting groups

Reporting group title	Synflorix Booster Group
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Reporting group description:

Subjects in this group had been previously primed with Synflorix™ and Infanrix™ hexa as part of the 10PN-PD-DIT-005 primary vaccination study, received in this study one dose of Havrix™ co-administered with one dose of Infanrix™ hexa at Month 0 (Dose 1) and one dose of Synflorix™ at Month 2 (Dose 2).

Reporting group title	Synflorix Catch-up Group
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Reporting group description:

Subjects in this group were subjects previously primed with Havrix™ and Infanrix™ hexa co-administered with Infanrix™ hexa as part of 10PN-PD-DIT-005 primary vaccination study and who received in this study a catch-up dose of Synflorix™ co-administered with Infanrix™ hexa at Month 0 (Dose 1) and one booster dose of Synflorix™ at Month 2 (Dose 2).

Reporting group values	Synflorix Booster Group	Synflorix Catch-up Group	Total
Number of subjects	84	79	163
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	84	79	163
Age continuous Units: months			
arithmetic mean	18.3	18.3	
standard deviation	± 0.44	± 0.5	-
Gender categorical Units: Subjects			
Female	39	44	83
Male	45	35	80

End points

End points reporting groups

Reporting group title	Synflorix Booster Group
Reporting group description: Subjects in this group had been previously primed with Synflorix™ and Infanrix™ hexa as part of the 10PN-PD-DIT-005 primary vaccination study, received in this study one dose of Havrix™ co-administered with one dose of Infanrix™ hexa at Month 0 (Dose 1) and one dose of Synflorix™ at Month 2 (Dose 2).	
Reporting group title	Synflorix Catch-up Group
Reporting group description: Subjects in this group were subjects previously primed with Havrix™ and Infanrix™ hexa co-administered with Infanrix™ hexa as part of 10PN-PD-DIT-005 primary vaccination study and who received in this study a catch-up dose of Synflorix™ co-administered with Infanrix™ hexa at Month 0 (Dose 1) and one booster dose of Synflorix™ at Month 2 (Dose 2).	

Primary: Number of subjects reporting grade 3 symptoms (solicited and unsolicited)

End point title	Number of subjects reporting grade 3 symptoms (solicited and unsolicited) ^[1]
End point description: Grade 3 symptoms are symptoms which prevent normal, everyday activities (e.g. in a young child such symptom would prevent attendance at school/ kindergarten/ a day-care center and would cause the parents/guardians to seek medical advice).	
End point type	Primary
End point timeframe: Within 4 days after the administration of any study vaccine dose	

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 Booster Group	Synflorix Catch-up Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	78		
Units: Subjects				
Any symptoms	32	36		
General symptoms	6	14		
Local symptoms	30	32		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local symptoms

End point title	Number of subjects reporting solicited local symptoms
End point description: Solicited local symptoms assessed include pain, redness and swelling	

End point type	Secondary
End point timeframe:	
Within 4 days after the administration of any study vaccine dose	

End point values	Synflorix Booster Group	Synflorix Catch-up Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	78		
Units: Subjects				
Pain	57	63		
Redness	49	52		
Swelling	44	47		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general symptoms

End point title	Number of subjects reporting solicited general symptoms
End point description:	
Solicited general symptoms assessed include drowsiness, fever, irritability and loss of appetite. Fever was defined as rectal temperature ≥ 38 degrees Celsius.	
End point type	Secondary
End point timeframe:	
Within 4 days after the administration of any study vaccine dose	

End point values	Synflorix Booster Group	Synflorix Catch-up Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	78		
Units: Subjects				
Drowsiness	33	36		
Fever	30	40		
Irritability	56	55		
Loss of appetite	35	37		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reporting unsolicited adverse events (AEs)
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End point description:

An Adverse Event 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.

End point type	Secondary
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End point timeframe:

Within 31 days after the administration of any study vaccine dose

End point values	Synflorix Booster Group	Synflorix Catch-up Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	79		
Units: Subjects				
Unsolicited AEs	47	47		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAEs) during the active phase of the study

End point title	Number of subjects reporting serious adverse events (SAEs) during the active phase of the study
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End point description:

A serious adverse event (SAE) is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

End point type	Secondary
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End point timeframe:

Throughout the active phase of the study, from Month 0 to Month 3 (Month 0/Dose 1 administration up to 1 month after the Dose 2 of vaccine)

End point values	Synflorix Booster Group	Synflorix Catch-up Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	79		
Units: Subjects				
SAEs	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAEs) throughout the entire study period

End point title	Number of subjects reporting serious adverse events (SAEs) throughout the entire study period
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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, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

End point type	Secondary
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End point timeframe:

Throughout the entire study period (from the beginning of the booster phase up to the end of the 6-month extended safety follow-up)

End point values	Synflorix Booster Group	Synflorix Catch-up Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	79		
Units: Subjects				
SAEs	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with vaccine pneumococcal serotype antibody concentrations above the cut-off value

End point title	Number of subjects with vaccine pneumococcal serotype antibody concentrations above the cut-off value
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End point description:

Anti-pneumococcal antibody cut-off value assessed was 0.20 microgram per milliliter (µg/mL). The vaccine pneumococcal serotypes assessed include 1, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F.

End point type	Secondary
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End point timeframe:

Before (pre) and at Month 3, or one month after the administration of Dose 2 (post)

End point values	Synflorix Booster Group	Synflorix Catch-up Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	73		
Units: Subjects				
Anti-1 Pre (N=79; 72)	43	1		
Anti-1 Post (N=78; 70)	78	70		
Anti-4 Pre (N=75; 73)	45	3		
Anti-4 Post (N=77; 70)	77	70		
Anti-5 Pre (N=76; 70)	58	7		
Anti-5 Post (N=78; 70)	77	70		
Anti-6A Pre (N=76; 72)	66	36		
Anti-6A Post (N=77; 70)	71	64		
Anti-6B Pre (N=76; 73)	55	1		
Anti-6B Post (N=78; 70)	76	59		
Anti-7F Pre (N=70; 68)	60	8		
Anti-7F Post (N=78; 70)	77	70		
Anti-9V Pre (N=78; 72)	71	6		
Anti-9V Post (N=79; 70)	79	69		
Anti-14 Pre (N=76; 71)	69	20		
Anti-14 Post (N=79; 70)	79	70		
Anti-18C Pre (N=77; 73)	68	5		
Anti-18C Post (N=78; 70)	78	70		
Anti-19A Pre (N=78; 73)	72	50		
Anti-19A Post (N=78; 70)	78	70		
Anti-19F Pre (N=80; 72)	76	19		
Anti-19F Post (N=78; 70)	78	70		
Anti-23F Pre (N=76; 71)	59	3		
Anti-23F Post (N=78; 70)	78	66		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with opsonophagocytic activity against vaccine pneumococcal serotypes above the cut-off value

End point title	Number of subjects with opsonophagocytic activity against vaccine pneumococcal serotypes above the cut-off value
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End point description:

Cut-off value for opsonophagocytic activity against pneumococcal antibody assessed was ≥ 8 The vaccine pneumococcal serotypes assessed include 1, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F.

End point type	Secondary
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End point timeframe:

Before (pre) and at Month 3, or one month after the administration of Dose 2 (post)

End point values	Synflorix Booster Group	Synflorix Catch-up Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	28		
Units: Subjects				
Opsono-1 Pre (N=28; 25)	12	1		
Opsono-1 Post (N=25; 25)	25	13		
Opsono-4 Pre (N=17; 19)	7	1		
Opsono-4 Post (N=24; 18)	24	18		
Opsono-5 Pre (N=19; 23)	13	1		
Opsono-5 Post (N=20; 25)	20	21		
Opsono-6A Pre (N=20; 25)	12	2		
Opsono-6A Post (N=19; 19)	14	12		
Opsono-6B Pre (N=22; 25)	12	3		
Opsono-6B Post (N=24; 27)	22	13		
Opsono-7F Pre (N=17; 12)	16	4		
Opsono-7F Post (N=25; 26)	25	26		
Opsono-9V Pre (N=20; 17)	20	11		
Opsono-9V Post (N=23; 23)	23	22		
Opsono-14 Pre (N=16; 11)	14	5		
Opsono-14 Post (N=21; 25)	21	25		
Opsono-18C Pre (N=29; 28)	12	3		
Opsono-18C Post (N=26; 27)	25	27		
Opsono-19A Pre (N=18; 18)	0	0		
Opsono-19A Post (N=23; 19)	14	5		
Opsono-19F Pre (N=22; 23)	17	2		
Opsono-19F Post (N=20; 21)	20	20		
Opsono-23F Pre (N=21; 16)	18	8		
Opsono-23F Post (N=25; 25)	25	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-protein D antibody concentrations above the cut-off value

End point title	Number of subjects with anti-protein D antibody concentrations above the cut-off value
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End point description:

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

End point type	Secondary
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End point timeframe:

Before (pre) and at Month 3, or one month after the administration of Dose 2 (post)

End point values	Synflorix Booster Group	Synflorix Catch-up Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	70		
Units: Subjects				
Pre (N= 73; 69)	72	44		
Post (N= 77; 70)	77	70		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-hepatitis A virus antibodies concentration

End point title	Anti-hepatitis A virus antibodies concentration
End point description:	Concentration of anti-hepatitis A antibodies given as geometric mean concentration (GMC) in milli-international units per milliliter (mIU/mL).
End point type	Secondary
End point timeframe:	Before (pre) and at Month 3, or one month after the administration of Dose 2 (post)

End point values	Synflorix Booster Group	Synflorix Catch-up Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Pre (N=18; 21)	30.3 (16.3 to 56.3)	539.9 (231 to 1261.9)		
Post (N=19; 19)	495.5 (228 to 1076.7)	478.5 (199.4 to 1148.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects With Anti-hepatitis A antibody concentrations above the cut-off value

End point title	Number of subjects With Anti-hepatitis A antibody concentrations above the cut-off value
End point description:	Anti-hepatitis A antibodies cut-off value assessed was ≥ 15 mIU/mL.
End point type	Secondary

End point timeframe:

Before (pre) and at Month 3, or one month after the administration of Dose 2 (post)

End point values	Synflorix Booster Group	Synflorix Catch-up Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Subjects				
Pre (N=18; 21)	12	21		
Post (N=19; 19)	18	19		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms and unsolicited : 4-day (Days 0-3) and 31-day (Days 0-30) follow-up periods post vaccination(s), across doses, respectively. SAEs : Month 0 to Month 8

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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.1
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Reporting groups

Reporting group title	Synflorix booster group
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Reporting group description:

Subjects in this group had been previously primed with Synflorix™ as part of the 10PN-PD-DIT-005 primary vaccination study, received in this study one dose of Havrix™ co-administered with one dose of Infanrix™ hexa at Month 0 (Dose 1) and one dose of Synflorix™ at Month 2 (Dose 2).

Reporting group title	Synflorix catch-up group
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Reporting group description:

Subjects in this group were subjects previously primed with Havrix™ co-administered with Infanrix™ hexa as part of 10PN-PD-DIT-005 primary vaccination study and who received in this study a catch-up dose of Synflorix™ co-administered with Infanrix™ hexa at Month 0 (Dose 1) and one booster dose of Synflorix™ at Month 2 (Dose 2)

Serious adverse events	Synflorix booster group	Synflorix catch-up group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 84 (1.19%)	0 / 79 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	1 / 84 (1.19%)	0 / 79 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Synflorix booster group	Synflorix catch-up group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 84 (92.86%)	75 / 79 (94.94%)	
General disorders and administration site conditions			
Injection site induration			
subjects affected / exposed	7 / 84 (8.33%)	7 / 79 (8.86%)	
occurrences (all)	7	7	
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	57 / 84 (67.86%)	63 / 79 (79.75%)	
occurrences (all)	57	63	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	49 / 84 (58.33%)	52 / 79 (65.82%)	
occurrences (all)	49	52	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	44 / 84 (52.38%)	47 / 79 (59.49%)	
occurrences (all)	44	47	
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	33 / 84 (39.29%)	36 / 79 (45.57%)	
occurrences (all)	33	36	
Fever (Rectally)			
alternative assessment type: Systematic			
subjects affected / exposed	30 / 84 (35.71%)	40 / 79 (50.63%)	
occurrences (all)	30	40	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	56 / 84 (66.67%)	55 / 79 (69.62%)	
occurrences (all)	56	55	
Loss of appetite			
alternative assessment type: Systematic			

subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	35 / 84 (41.67%) 35 4 / 84 (4.76%) 4	37 / 79 (46.84%) 37 5 / 79 (6.33%) 5	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	6 / 84 (7.14%) 6 5 / 84 (5.95%) 5	8 / 79 (10.13%) 8 2 / 79 (2.53%) 2	
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all)	15 / 84 (17.86%) 15 6 / 84 (7.14%) 6 5 / 84 (5.95%) 5 6 / 84 (7.14%) 6	16 / 79 (20.25%) 16 14 / 79 (17.72%) 14 4 / 79 (5.06%) 4 8 / 79 (10.13%) 8	

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