Clinical trial results:
Phase II, double blind, randomized, comparative study of the immunogenicity and safety of GlaxoSmithKline Biologicals' modified formulation varicella vaccine and Varilrix™ given as a 2 dose course in the second year of life

Summary

EudraCT number	2007-000683-24
Trial protocol	CZ HU
Global end of trial date	29 April 2008

Results information

Result version number	v1
This version publication date	27 April 2016
First version publication date	31 July 2015

Trial information

Trial identification

Sponsor protocol code	109705

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00568334
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 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 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?	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 October 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 March 2008
Global end of trial reached?	Yes
Global end of trial date	29 April 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of Varilrix HSA-free vaccine as compared to Varilrix vaccine in terms of geometric mean titer (GMT) of varicella zoster virus (VZV) antibodies 43-57 days after the first dose vaccination.
Criterion for non-inferiority: The lower limit of the 95% confidence interval (CI) for the GMT ratio (derived from immunofluorescence assay [IFA]) between Group Varilrix HSA free and (divided by) Group Varilrix is equal to or above the pre-defined clinical limit of 0.5.
If this first criterion was met, an additional criterion was to be tested.
Additional criterion of non-inferiority: The lower limit of the 95% CI for the GMC ratio (derived from ELISA) between Group Varilrix HSA-free and (divided by) Group Varilrix is equal to or above the pre-defined clinical limit of 0.67

Protection of trial subjects:

The subjects were observed closely for at least 30 minutes following the administration of vaccines, with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 November 2007
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	Czech Republic: 114
Country: Number of subjects enrolled	Hungary: 130
Worldwide total number of subjects	244
EEA total number of subjects	244

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)	244

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:

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 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	HSAFREE Group

Arm description:

Subjects received 2 doses of GSK Biologicals' live attenuated varicella vaccine produced without human serum albumin (OKAH HSA-free).

Arm type	Experimental
Investigational medicinal product name	Varilrix HSA-free
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Two doses of OKAH HSA-free vaccine administered subcutaneously into the left upper arm (deltoid region) on Day 0 and Week 6 (Day 43-57).

Arm title	OKAH Group

Arm description:

Subjects received 2 doses of GSK Biologicals' live attenuated varicella vaccine (OKAH).

Arm type	Experimental
Investigational medicinal product name	Varilrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Two doses of OKAH vaccine administered subcutaneously into the left upper arm (deltoid region) on Day 0 and Week 6 (Day 43-57).

Number of subjects in period 1	HSAFREE Group	OKAH Group
Started	122	122
Completed	121	121
Not completed	1	1
Consent withdrawn by subject	-	1
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	HSAFREE Group
Reporting group description:	
Subjects received 2 doses of GSK Biologicals' live attenuated varicella vaccine produced without human serum albumin (OKAH HSA-free).	
Reporting group title	OKAH Group
Reporting group description:	
Subjects received 2 doses of GSK Biologicals' live attenuated varicella vaccine (OKAH).	

Reporting group values	HSAFREE Group	OKAH Group	Total
Number of subjects	122	122	244
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	15.6	14.8	
standard deviation	± 3.34	± 3.08	-
Gender categorical			
Units: Subjects			
Female	59	60	119
Male	63	62	125

End points

End points reporting groups

Reporting group title	HSAFREE Group
Reporting group description:	
Subjects received 2 doses of GSK Biologicals' live attenuated varicella vaccine produced without human serum albumin (OKAH HSA-free).	
Reporting group title	OKAH Group
Reporting group description:	
Subjects received 2 doses of GSK Biologicals' live attenuated varicella vaccine (OKAH).	

Primary: Antibody titers against the varicella zoster virus (VZV) by Immunofluorescence Assay [IFA]

End point title	Antibody titers against the varicella zoster virus (VZV) by Immunofluorescence Assay [IFA]
End point description:	
Antibody titers were summarized by geometric mean titers (GMTs) with their 95% CIs.	
End point type	Primary
End point timeframe:	
At 43-57 days after the first vaccination dose (Week 6).	

End point values	HSAFREE Group	OKAH Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	115		
Units: Titer				
geometric mean (confidence interval 95%)				
anti-VZV	172.6 (141.6 to 210.3)	154.3 (128.7 to 185)		

Statistical analyses

Statistical analysis title	Non-inferiority of HSAFREEcompared to OKAH vaccine
Statistical analysis description:	
Non-inferiority of HSAFREE vaccine as compared to OKAH vaccine in terms of geometric mean titers (GMTs) of varicella zoster virus (VZV) antibodies 43-57 days after the first dose vaccination. The lower limit of the 95% confidence interval (CI) for the GMT ratio (derived from IFA) between Group HSAFREE and (divided by) Group OKAH is equal to or above the pre-defined clinical limit of 0.5.	
Comparison groups	HSAFREE Group v OKAH Group

Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.46

Primary: Antibody titers against the varicella zoster virus (VZV) by enzyme-linked immunosorbent assay [ELISA]

End point title	Antibody titers against the varicella zoster virus (VZV) by enzyme-linked immunosorbent assay [ELISA]

End point description:

Antibody titers were summarized by geometric mean concentrations (GMCs) with their 95% CIs.

End point type	Primary

End point timeframe:

At 43-57 days after the first vaccination dose (Week 6).

End point values	HSAFREE Group	OKAH Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	115		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
anti-VZV	123.5 (107.9 to 141.4)	110.7 (98.4 to 124.6)		

Statistical analyses

Statistical analysis title	Non-inferiority of HSAFREEcompared to OKAH vaccine

Statistical analysis description:

Non-inferiority of HSAFREE vaccine as compared to OKAH vaccine in terms of geometric mean concentrations (GMCs) of varicella zoster virus (VZV) antibodies 43-57 days after the first dose vaccination. The lower limit of the 95% CI for the GMC ratio (derived from ELISA) between Group HSAFREE and (divided by) Group OKAH is equal to or above the pre-defined clinical limit of 0.67.

Comparison groups	HSAFREE Group v OKAH Group

Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMC Ratio
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.33

Secondary: Number of subjects seroconverted for varicella antibodies above the cut-off value

End point title	Number of subjects seroconverted for varicella antibodies above the cut-off value

End point description:

Seroconversion/seroresponse (considering the IFA data) was defined as the appearance of anti VZV antibodies (i.e. titer/concentration greater than or equal to the assay cut-off value e.g. antibody titer ≥ 1:4) in the sera of subjects who were seronegative before vaccination.

End point type	Secondary

End point timeframe:

At 43-57 days post dose 1 (Week 6) and 86-114 days post dose 2 (Week 12)

End point values	HSAFREE Group	OKAH Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	115		
Units: Subjects				
anti-VZV ≥ 1:4 [N=116,115]; Week 6	114	114		
anti-VZV ≥ 1:4 [N=115,112]; Week 12	115	112		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted for varicella antibodies above the cut-off value

End point title	Number of subjects seroconverted for varicella antibodies above the cut-off value

End point description:

Seroconversion/seroresponse (considering the ELISA data) was defined as the appearance of anti VZV antibodies (i.e. titer/concentration greater than or equal to the assay cut-off value e.g. antibody concentration ≥ 25 mIU/mL) in the sera of subjects who were seronegative before vaccination.

End point type	Secondary

End point timeframe:

At 43-57 days post dose 1 (Week 6) and 86-114 days post dose 2 (Week 12)

End point values	HSAFREE Group	OKAH Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	115		
Units: Subjects				
anti-VZV ≥ 25 mIU/mL [N=116,115]; Week 6	114	113		
anti-VZV ≥ 25 mIU/mL [N=116,114]; Week 12	116	114		
anti-VZV ≥ 50 mIU/mL [N=116,115]; Week 6	105	103		
anti-VZV ≥ 50 mIU/mL [N=116,114]; Week 12	116	114		
anti-VZV ≥ 75 mIU/mL [N=116,115]; Week 6	89	89		
anti-VZV ≥ 75 mIU/mL [N=116,114]; Week 12	116	114		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers against the varicella zoster virus (VZV) by Immunofluorescence Assay [IFA]

End point title	Antibody titers against the varicella zoster virus (VZV) by Immunofluorescence Assay [IFA]

End point description:

Antibody titers were summarized by geometric mean titers (GMTs) with their 95% CIs.

End point type	Secondary

End point timeframe:

At 86-114 days after the second vaccination dose (Week 12).

End point values	HSAFREE Group	OKAH Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	112		
Units: Titers				
geometric mean (confidence interval 95%)				
anti-VZV	1452.5 (1240.7 to 1700.5)	1395.4 (1183 to 1645.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers against the varicella zoster virus (VZV) by enzyme-linked immunosorbent assay [ELISA]

End point title	Antibody titers against the varicella zoster virus (VZV) by enzyme-linked immunosorbent assay [ELISA]

End point description:

Antibody titers were summarized by geometric mean titers (GMTs) with their 95% CIs.

End point type	Secondary

End point timeframe:

At 86-114 days after the second vaccination dose (Week 12).

End point values	HSAFREE Group	OKAH Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	114		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
anti-VZV	1013.6 (880.9 to 1166.4)	999.2 (877.3 to 1138.1)		

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:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = Cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 20 millimeters (mm) of injection site.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose (Dose 1 and Dose 2)

End point values	HSAFREE Group	OKAH Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121	122		
Units: Subjects				
Any Pain; Dose 1	13	15		
Grade 3 Pain; Dose 1	0	0		
Any Redness; Dose 1	33	34		
Grade 3 Redness; Dose 1	0	0		

Any Swelling; Dose 1	5	7		
Grade 3 Swelling; Dose 1	0	0		
Any Pain; Dose 2	23	18		
Grade 3 Pain; Dose 2	0	0		
Any Redness; Dose 2	44	46		
Grade 3 Redness; Dose 2	6	3		
Any Swelling; Dose 2	18	14		
Grade 3 Swelling; Dose 2	2	2		

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:

Assessed solicited general symptoms were fever and rash. Any = occurrence of the symptom regardless of intensity grade and relationship to vaccination. Any fever was defined as fever ≥ 37.5°C and grade 3 fever > 39.0°C after vaccination. Grade 3 rash = > 150 lesions. Related = considered by the investigator to be causally related to the study vaccination.

End point type	Secondary

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period following each dose (Dose 1 and Dose 2)

End point values	HSAFREE Group	OKAH Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121	122		
Units: Subjects				
Any temperature; Dose 1	64	52		
Grade 3 temperature; Dose 1	13	11		
Any rash; Dose 1	2	2		
Grade 3 rash; Dose 1	1	0		
Any temperature; Dose 2	54	53		
Grade 3 temperature; Dose 2	6	12		
Any rash; Dose 2	3	3		
Grade 3 rash; Dose 2	1	0		
Related temperature; Dose 1	31	18		
Related rash; Dose 1	0	0		
Related temperature; Dose 2	31	23		
Related rash; Dose 2	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse event (AE)

End point title	Number of subjects reporting any unsolicited adverse event (AE)

End point description:

An unsolicited AE covers 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 was defined as an adverse event (AE) reported in addition to those solicited during the clinical study. Any solicited symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event.

End point type	Secondary

End point timeframe:

Within the 43-day (Days 0-42) post-vaccination period after Dose 1.

End point values	HSAFREE Group	OKAH Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	122		
Units: Subjects				
any AE(s)	56	45		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse event (AE)

End point title	Number of subjects reporting any unsolicited adverse event (AE)

End point description:

An unsolicited AE covers 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 was defined as an adverse event (AE) reported in addition to those solicited during the clinical study. Any solicited symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event.

End point type	Secondary

End point timeframe:

Within the 43-day (Days 0-42) post-vaccination period after Dose 2

End point values	HSAFREE Group	OKAH Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121	121		
Units: Subjects				
any AE(s)	35	42		

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:

Serious adverse events (SAEs) assessed include medical occurrences that results in death, are life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity or is a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

From Day 0 up to study end (Day 86-114)

End point values	HSAFREE Group	OKAH Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	121		
Units: Subjects				
any SAE(s)	2	5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local symptoms were collected during the 4-day (Days 0-3) post each dose. Solicited general symptoms and unsolicited AEs during the 43-day (Days 0-42) post each dose. SAEs were collected during the entire study period (Day 0 to Day 86/114).

Adverse event reporting additional description:

The number of occurrences reported for serious adverse events were not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups

Reporting group title	HSAFREE Group

Reporting group description:

Subjects received 2 doses of GSK Biologicals' live attenuated varicella vaccine produced without human serum albumin (OKAH HSA-free) vaccine

Reporting group title	OKAH Group

Reporting group description:

Subjects received 2 doses of GSK Biologicals' live attenuated varicella vaccine (OKAH) vaccine

Serious adverse events	HSAFREE Group	OKAH Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 122 (1.64%)	5 / 122 (4.10%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Concussion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 122 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Breath holding			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 122 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Otitis media			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 122 (0.82%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 122 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 122 (0.82%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 122 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastoiditis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 122 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 122 (0.00%)	1 / 122 (0.82%)	
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	HSAFREE Group	OKAH Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 122 (52.46%)	53 / 122 (43.44%)	
General disorders and administration site conditions			
Pain; Dose 1			
subjects affected / exposed[1]	13 / 121 (10.74%)	15 / 122 (12.30%)	
occurrences (all)	13	15	
Redness; Dose 1			
subjects affected / exposed[2]	33 / 121 (27.27%)	34 / 122 (27.87%)	
occurrences (all)	33	34	
Swelling; Dose 1			
subjects affected / exposed[3]	5 / 121 (4.13%)	7 / 122 (5.74%)	
occurrences (all)	5	7	
Pain; Dose 2			
subjects affected / exposed[4]	23 / 121 (19.01%)	18 / 121 (14.88%)	
occurrences (all)	23	18	
Redness; Dose 2			
subjects affected / exposed[5]	44 / 121 (36.36%)	46 / 121 (38.02%)	
occurrences (all)	44	46	
Swelling; Dose 2			
subjects affected / exposed[6]	18 / 121 (14.88%)	14 / 121 (11.57%)	
occurrences (all)	18	14	
Fever; Dose 1			
subjects affected / exposed[7]	64 / 121 (52.89%)	52 / 122 (42.62%)	
occurrences (all)	64	52	
Fever; Dose 2			
subjects affected / exposed[8]	54 / 121 (44.63%)	53 / 121 (43.80%)	
occurrences (all)	54	53	
Infections and infestations			
Bronchitis; Dose 1			
alternative assessment type: Non-systematic			
subjects affected / exposed	15 / 122 (12.30%)	8 / 122 (6.56%)	
occurrences (all)	15	8	
Viral infection; Dose 1			
alternative assessment type: Non-systematic			

subjects affected / exposed	11 / 122 (9.02%)	11 / 122 (9.02%)	
occurrences (all)	11	11	
Rhinitis; Dose 1			
subjects affected / exposed	6 / 122 (4.92%)	8 / 122 (6.56%)	
occurrences (all)	6	8	
Bronchitis; Dose 2			
alternative assessment type: Non-systematic			
subjects affected / exposed[9]	8 / 121 (6.61%)	11 / 121 (9.09%)	
occurrences (all)	8	11	
Viral infection; Dose 2			
alternative assessment type: Non-systematic			
subjects affected / exposed[10]	6 / 121 (4.96%)	13 / 121 (10.74%)	
occurrences (all)	6	13	
Rhinitis; Dose 2			
alternative assessment type: Non-systematic			
subjects affected / exposed[11]	7 / 121 (5.79%)	1 / 121 (0.83%)	
occurrences (all)	7	1	

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: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects/doses with documented safety data (i.e. symptom screen/sheet 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: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects/doses with documented safety data (i.e. symptom screen/sheet 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: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort will include only subjects/doses with documented safety data (i.e. symptom screen/sheet 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: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects/doses with documented safety data (i.e. symptom screen/sheet 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: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects/doses with documented safety data (i.e. symptom screen/sheet 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: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects/doses with documented safety data (i.e. symptom screen/sheet completed).

[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: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects/doses with documented safety data (i.e. symptom screen/sheet completed).
[8] - 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: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort will include only subjects/doses with documented safety data (i.e. symptom screen/sheet completed).
[9] - 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: For the analysis of unsolicited adverse events/serious adverse event/concomitant medication, all vaccinated subjects were considered and subjects who did not report an event were considered as subjects without an event.
[10] - 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: For the analysis of unsolicited adverse events/serious adverse event/concomitant medication, all vaccinated subjects were considered and subjects who did not report an event were considered as subjects without an event.
[11] - 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: For the analysis of unsolicited adverse events/serious adverse event/concomitant medication, all vaccinated subjects were considered and subjects who did not report an event were considered as subjects without an event.

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