



Clinical trial results:

A Phase III, randomised, partially-blind, controlled, multi-centric, multi-country study to evaluate the immunogenicity, safety and reactogenicity of GSK Biologicals' MenACWY-TT conjugate vaccine co-administered with Boostrix® administered intramuscularly versus MenACWY-TT alone administered intramuscularly, in healthy adolescents and young adults between 11 and 25 years of age.

Summary

EudraCT number	2012-002737-11
Trial protocol	DE
Global end of trial date	16 January 2014

Results information

Result version number	v2 (current)
This version publication date	19 August 2017
First version publication date	06 March 2015
Version creation reason	• New data added to full data set Addition to primary and secondary outcomes

Trial information

Trial identification

Sponsor protocol code	116705
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01767376
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, 1330
Public contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, 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?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	11 November 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 January 2014
Global end of trial reached?	Yes
Global end of trial date	16 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To demonstrate the non-inferiority of MenACWY-TT co-administered with Boostrix compared to MenACWY-TT administered alone with respect to serum bactericidal assay using rabbit complement (rSBA) geometric mean titres (GMTs) for serogroups A, C, W-135 and Y one month after MenACWY-TT vaccination.
- To demonstrate the non-inferiority of Boostrix co-administered with MenACWY-TT compared to Boostrix administered alone in terms of anti-diphtheria toxoid (anti-D) and anti-tetanus toxoid (anti-T) antibody concentrations one month after Boostrix vaccination.
- To demonstrate the non-inferiority of Boostrix co-administered with MenACWY-TT compared to Boostrix administered alone with respect to geometric mean concentrations (GMCs) to each discrete pertussis antigen (pertussis toxoid [PT], filamentous haemagglutinin [FHA] and pertactin [PRN]) one month after Boostrix vaccination.

Protection of trial subjects:

All subjects were supervised after vaccination/product administration 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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 January 2013
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: 181
Country: Number of subjects enrolled	Dominican Republic: 180
Country: Number of subjects enrolled	Korea, Republic of: 331
Worldwide total number of subjects	692
EEA total number of subjects	181

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)	78
Adolescents (12-17 years)	211
Adults (18-64 years)	403
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Out of the 692 subjects enrolled in this study, one subject was eliminated due to not receiving vaccination, hence only 691 subject started the study.

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.

Pre-assignment period milestones

Number of subjects started	692
Number of subjects completed	691

Pre-assignment subject non-completion reasons

Reason: Number of subjects	No vaccination received: 1
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Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
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Arm title	Nimenrix+Boostrix Group
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Arm description:

Healthy male or female subjects, between and including 11 and 25 years of age, who received one dose of Nimenrix vaccine co-administered with one dose of Boostrix vaccine at Month 0.

Arm type	Experimental
Investigational medicinal product name	Nimenrix
Investigational medicinal product code	
Other name	Meningococcal vaccine GSK134612
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered intramuscularly (IM) in the deltoid muscle of the arm at Month 0.

Investigational medicinal product name	Boostrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered intramuscularly (IM) in the deltoid of the right arm at Month 0.

Arm title	Nimenrix Group
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Arm description:

Healthy male or female subjects, between and including 11 and 25 years of age, who received one dose of Nimenrix vaccine at Month 0 and one dose of Boostrix vaccine at Month 1.

Arm type	Experimental
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Investigational medicinal product name	Nimenrix
Investigational medicinal product code	
Other name	Meningococcal vaccine GSK134612
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
One dose administered intramuscularly (IM) in the deltoid muscle of the arm at Month 0.	
Investigational medicinal product name	Boostrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
One dose administered intramuscularly (IM) in the deltoid of the left arm at Month 1.	
Arm title	Boostrix Group
Arm description:	
Healthy male or female subjects, between and including 11 and 25 years of age, who received one dose of Boostrix vaccine at Month 0 and one dose of Nimenrix vaccine at Month 1.	
Arm type	Experimental
Investigational medicinal product name	Nimenrix
Investigational medicinal product code	
Other name	Meningococcal vaccine GSK134612
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
One dose administered intramuscularly (IM) in the deltoid muscle of the arm at Month 1.	
Investigational medicinal product name	Boostrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
One dose administered intramuscularly (IM) in the deltoid of the left arm at Month 0.	

Number of subjects in period 1^[1]	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group
Started	231	228	232
Completed	227	225	232
Not completed	4	3	0
Consent withdrawn by subject	1	1	-
Lost to follow-up	3	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: Out of the 692 subjects enrolled in this study, one subject was eliminated due to not receiving vaccination, hence only 691 subject started the study.

Baseline characteristics

Reporting groups

Reporting group title	Nimenrix+Boostrix Group
Reporting group description:	
Healthy male or female subjects, between and including 11 and 25 years of age, who received one dose of Nimenrix vaccine co-administered with one dose of Boostrix vaccine at Month 0.	
Reporting group title	Nimenrix Group
Reporting group description:	
Healthy male or female subjects, between and including 11 and 25 years of age, who received one dose of Nimenrix vaccine at Month 0 and one dose of Boostrix vaccine at Month 1.	
Reporting group title	Boostrix Group
Reporting group description:	
Healthy male or female subjects, between and including 11 and 25 years of age, who received one dose of Boostrix vaccine at Month 0 and one dose of Nimenrix vaccine at Month 1.	

Reporting group values	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group
Number of subjects	231	228	232
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	18.1	18.2	18.3
standard deviation	± 4.2	± 4.5	± 4.4
Gender categorical Units: Subjects			
Female	128	126	146
Male	103	102	86

Reporting group values	Total		
Number of subjects	691		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years)	0 0 0 0 0		

Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	400		
Male	291		

End points

End points reporting groups

Reporting group title	Nimenrix+Boostrix Group
Reporting group description: Healthy male or female subjects, between and including 11 and 25 years of age, who received one dose of Nimenrix vaccine co-administered with one dose of Boostrix vaccine at Month 0.	
Reporting group title	Nimenrix Group
Reporting group description: Healthy male or female subjects, between and including 11 and 25 years of age, who received one dose of Nimenrix vaccine at Month 0 and one dose of Boostrix vaccine at Month 1.	
Reporting group title	Boostrix Group
Reporting group description: Healthy male or female subjects, between and including 11 and 25 years of age, who received one dose of Boostrix vaccine at Month 0 and one dose of Nimenrix vaccine at Month 1.	

Primary: Anti-Meningitis antibody titers by serum bactericidal assay using rabbit complement (rSBA)

End point title	Anti-Meningitis antibody titers by serum bactericidal assay using rabbit complement (rSBA) ^[1]
End point description: The analysis was performed for the serogroups -MenA, -MenC -MenW-135 and -MenY. Antibody titers tabulated as geometric mean titers (GMTs), were obtained by serum bactericidal assay using rabbit complement.	
End point type	Primary
End point timeframe: At one month after Nimenrix vaccination	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Because of splitting into primary/secondary end points for some of the groups, the results were presented separately.

End point values	Nimenrix+Boostrix Group	Nimenrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226	222		
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA (N=225;222)	3415.3 (2917.8 to 3997.6)	2860.4 (2478.6 to 3300.9)		
rSBA-MenC (N=226;222)	5092.5 (4268.7 to 6075.3)	4597.6 (3703.1 to 5708.2)		
rSBA-MenW-135 (N=226;222)	9608.5 (8522.5 to 10832.8)	9052.8 (7510.3 to 10912)		
rSBA-MenY (N=226;222)	7775.8 (6862.3 to 8811)	6032.6 (5025.7 to 7241.2)		

Statistical analyses

Statistical analysis title	Difference in adjusted GMT ratio for rSBA-MenA
Statistical analysis description:	
To demonstrate that the immunogenicity of Nimenrix vaccine co-administered with Boostrix vaccine (Nimenrix+Boostrix Group) was non-inferior to that of Nimenrix vaccine administered alone (Nimenrix Group) at Month 0, with respect to serum bactericidal assay using rabbit complement (rSBA) geometric mean titers (GMTs) for serogroup A, at one month after the Nimenrix vaccination.	
Comparison groups	Nimenrix+Boostrix Group v Nimenrix Group
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[2]
Method	ANCOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.48

Notes:

[2] - Non-inferiority was defined as the lower limit (LL) of the two-sided standardised asymptotic 95% confidence interval (CI) for rSBA GMT ratios for serogroup A between the two groups (Nimenrix+Boostrix Group minus Nimenrix Group) being greater than or equal to (\geq) the pre-defined limit of 0.5.

Statistical analysis title	Difference in adjusted GMT ratio for rSBA-MenC
Statistical analysis description:	
To demonstrate that the immunogenicity of Nimenrix vaccine co-administered with Boostrix vaccine (Nimenrix+Boostrix Group) was non-inferior to that of Nimenrix vaccine administered alone (Nimenrix Group) at Month 0, with respect to serum bactericidal assay using rabbit complement (rSBA) geometric mean titers (GMTs) for serogroup C, at one month after the Nimenrix vaccination.	
Comparison groups	Nimenrix+Boostrix Group v Nimenrix Group
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
Method	ANCOVA
Parameter estimate	Adjusted GMT ratio
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.47

Notes:

[3] - Non-inferiority was defined as the lower limit (LL) of the two-sided standardised asymptotic 95% confidence interval (CI) for rSBA GMT ratios for serogroup C between the two groups (Nimenrix+Boostrix Group minus Nimenrix Group) being greater than or equal (\geq) to the pre-defined limit of 0.5.

Statistical analysis title	Difference in adjusted GMT ratio for rSBA-MenW-135
Statistical analysis description:	
To demonstrate that the immunogenicity of Nimenrix vaccine co-administered with Boostrix vaccine (Nimenrix+Boostrix Group) was non-inferior to that of Nimenrix vaccine administered alone (Nimenrix Group) at Month 0, with respect to serum bactericidal assay using rabbit complement (rSBA) geometric mean titers (GMTs) for serogroup W-135, at one month after the Nimenrix vaccination.	
Comparison groups	Nimenrix+Boostrix Group v Nimenrix Group
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[4]
Method	ANCOVA
Parameter estimate	Adjusted GMT ratio
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.32

Notes:

[4] - Non-inferiority was defined as the lower limit (LL) of the two-sided standardised asymptotic 95% confidence interval (CI) for rSBA GMT ratios for serogroup W-135 between the two groups (Nimenrix+Boostrix Group minus Nimenrix Group) being greater than or equal (\geq) to the pre-defined limit of 0.5.

Statistical analysis title	Difference in adjusted GMT ratio for rSBA-MenY
Statistical analysis description:	
To demonstrate that the immunogenicity of Nimenrix vaccine co-administered with Boostrix vaccine (Nimenrix+Boostrix Group) was non-inferior to that of Nimenrix vaccine administered alone (Nimenrix Group) at Month 0, with respect to serum bactericidal assay using rabbit complement (rSBA) geometric mean titers (GMTs) for serogroup Y, at one month after the Nimenrix vaccination.	
Comparison groups	Nimenrix+Boostrix Group v Nimenrix Group
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[5]
Method	ANCOVA
Parameter estimate	Adjusted GMT ratio
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.59

Notes:

[5] - Non-inferiority was defined as the lower limit (LL) of the two-sided standardised asymptotic 95% confidence interval (CI) for rSBA GMT ratios for serogroup Y between the two groups (Nimenrix+Boostrix Group minus Nimenrix Group) being greater than or equal (\geq) to the pre-defined limit of 0.5.

Primary: Number of subjects with anti-D and anti-T concentrations \geq 1.0 International Units per milliliter (IU/mL)

End point title	Number of subjects with anti-D and anti-T concentrations \geq 1.0 International Units per milliliter (IU/mL) ^[6]
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End point description:

The antibody concentrations were calculated as geometric mean concentrations (GMCs) and expressed as International Units per milliliter (IU/mL).

End point type	Primary
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End point timeframe:

At one month after Boostrix vaccination

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Because of splitting into primary/secondary end points for some of the groups, the results were presented separately.

End point values	Nimenrix+Boostrix Group	Boostrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	223		
Units: Subjects				
Anti-D	200	224		
Anti-T	203	223		

Statistical analyses

Statistical analysis title	Difference in percentage for anti-D antibodies
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Statistical analysis description:

To demonstrate that the immunogenicity of Boostrix vaccine co-administered with Nimenrix vaccine (Nimenrix+Boostrix Group) was non-inferior to that of Boostrix vaccine administered alone (Boostrix Group) at Month 0, in terms of percentage of subjects with anti-D antibody concentrations ≥ 1.0 International Units/mL (IU/mL), at one month after the Boostrix vaccination.

Comparison groups	Nimenrix+Boostrix Group v Boostrix Group
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[7]
Parameter estimate	Difference in percentage
Point estimate	-2.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.88
upper limit	3.53

Notes:

[7] - Non-inferiority was defined as the lower limit (LL) of the two-sided standardised asymptotic 95% confidence interval (CI) between the two groups (Nimenrix+Boostrix Group minus Boostrix Group), in terms of percentage of subjects with anti-D concentrations ≥ 1.0 IU/mL, being greater than or equal to (\geq) the pre-defined limit of -10%.

Statistical analysis title	Difference in percentage for anti-T antibodies
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Statistical analysis description:

To demonstrate that the immunogenicity of Boostrix vaccine co-administered with Nimenrix vaccine (Nimenrix+Boostrix Group) was non-inferior to that of Boostrix vaccine administered alone (Boostrix Group) at Month 0, in terms of percentage of subjects with anti-T antibody concentrations ≥ 1.0 IU/mL, at one month after the Boostrix vaccination.

Comparison groups	Nimenrix+Boostrix Group v Boostrix Group
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Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[8]
Parameter estimate	Difference in percentage
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.48
upper limit	1.26

Notes:

[8] - Non-inferiority was defined as the lower limit (LL) of the two-sided standardised asymptotic 95% confidence interval (CI) between the two groups (Nimenrix+Boostrix Group minus Boostrix Group), in terms of percentage of subjects with anti-T concentrations ≥ 1.0 IU/mL, being greater than or equal to (\geq) the pre-defined limit of -10%.

Primary: Anti-PT, anti-FHA and anti-PRN antibody concentrations

End point title	Anti-PT, anti-FHA and anti-PRN antibody concentrations ^[9]
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End point description:

The antibody concentrations were tabulated as geometric mean concentrations (GMCs) and expressed as International Units per milliliter (IU/mL).

End point type	Primary
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End point timeframe:

At one month after Boostrix vaccination

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Because of splitting into primary/secondary end points for some of the groups, the results were presented separately.

End point values	Nimenrix+Boostrix Group	Boostrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	223		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-PT (N=225;223)	53.6 (47.2 to 60.8)	68 (59.9 to 77.3)		
Anti-FHA (N=225;223)	316.9 (288 to 348.6)	545 (493.2 to 602.4)		
Anti-PRN (N=224;221)	348.3 (293.8 to 412.9)	499 (419.4 to 593.6)		

Statistical analyses

Statistical analysis title	Difference in adjusted GMC ratios for anti-PT
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Statistical analysis description:

To demonstrate that the immunogenicity of Boostrix vaccine co-administered with Nimenrix vaccine (Nimenrix+Boostrix Group) was non-inferior to that of Boostrix vaccine administered alone (Boostrix Group) at Month 0, with respect to geometric mean concentrations (GMCs) to pertussis antigen (PT), at one month after the Boostrix vaccination.

Comparison groups	Nimenrix+Boostrix Group v Boostrix Group
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Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[10]
Method	ANCOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.89

Notes:

[10] - Non-inferiority was defined as the lower limit (LL) of the two-sided standardised asymptotic 95% confidence interval (CI) between the two groups (Nimenrix+Boostrix Group minus Boostrix Group) for GMC ratios of antibodies against the pertussis (PT) antigen, being greater than or equal to (\geq) the pre-defined limit of 0.67.

Statistical analysis title	Difference in adjusted GMC ratios for anti-FHA
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Statistical analysis description:

To demonstrate that the immunogenicity of Boostrix vaccine co-administered with Nimenrix vaccine (Nimenrix+Boostrix Group) was non-inferior to that of Boostrix vaccine administered alone (Boostrix Group) at Month 0, with respect to geometric mean concentrations (GMCs) to filamentous haemagglutinin (FHA) antigen, at one month after the Boostrix vaccination.

Comparison groups	Nimenrix+Boostrix Group v Boostrix Group
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[11]
Method	ANCOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	0.65

Notes:

[11] - Non-inferiority was defined as the lower limit (LL) of the two-sided standardised asymptotic 95% confidence interval (CI) between the two groups (Nimenrix+Boostrix Group minus Boostrix Group) for GMC ratios of antibodies against the filamentous haemagglutinin (FHA) antigen, being greater than or equal to (\geq) the pre-defined limit of 0.67.

Statistical analysis title	Difference in adjusted GMC ratios for anti-PRN
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Statistical analysis description:

To demonstrate that the immunogenicity of Boostrix vaccine co-administered with Nimenrix vaccine (Nimenrix+Boostrix Group) was non-inferior to that of Boostrix vaccine administered alone (Boostrix Group) at Month 0, with respect to geometric mean concentrations (GMCs) to pertactin (PRN) antigen, at one month after the Boostrix vaccination.

Comparison groups	Nimenrix+Boostrix Group v Boostrix Group
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[12]
Method	ANCOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	0.72

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.88

Notes:

[12] - Non-inferiority was defined as the lower limit (LL) of the two-sided standardised asymptotic 95% confidence interval (CI) between the two groups (Nimenrix+Boostrix Group minus Boostrix Group) for GMC ratios of antibodies against the pertactin (PRN) antigen, being greater than or equal to (\geq) the pre-defined limit of 0.67.

Secondary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titres \geq 1:8 and \geq 1:128

End point title	Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titres \geq 1:8 and \geq 1:128
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End point description:

The number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers \geq 1:8 and \geq 1:128 is reported.

End point type	Secondary
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End point timeframe:

Prior to (PRE) and one month (POST) after Nimenrix vaccination

End point values	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	226	222	223	
Units: Subjects				
rSBA-MenA \geq 1:8, PRE (N=226;222;223)	92	92	76	
rSBA-MenA \geq 1:8, POST (N=225;222;223)	225	221	222	
rSBA-MenC \geq 1:8, PRE (N=226;222;223)	35	47	43	
rSBA-MenC \geq 1:8, POST (N=226;222;223)	225	220	222	
rSBA-MenW-135 \geq 1:8, PRE (N=226;222;223)	34	36	26	
rSBA-MenW-135 \geq 1:8, POST (N=226;222;223)	226	220	216	
rSBA-MenY \geq 1:8, PRE (N=226;222;223)	93	67	74	
rSBA-MenY \geq 1:8, POST (N=226;222;223)	226	220	222	
rSBA-MenA \geq 1:128, PRE (N=226;222;223)	48	46	33	
rSBA-MenA \geq 1:128, POST (N=225;222;223)	224	220	220	
rSBA-MenC \geq 1:128, PRE (N=226;222;223)	13	33	30	
rSBA-MenC \geq 1:128, POST (N=226;222;223)	225	218	220	
rSBA-MenW-135 \geq 1:128, PRE (N=226;222;223)	31	29	23	
rSBA-MenW-135 \geq 1:128, POST (N=226;222;223)	226	220	216	

rSBA-MenY \geq 1:128, PRE (N=226;222;223)	80	56	70	
rSBA-MenY \geq 1:128, POST (N=226;222;223)	226	219	222	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PT, anti-FHA and anti-PRN antibody concentrations above the cut-off values

End point title	Number of subjects with anti-PT, anti-FHA and anti-PRN antibody concentrations above the cut-off values
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End point description:

The cut-off values assessed were greater than or equal (\geq) to 5 International units per milliliter (IU/mL) in the sera of subjects seronegative before vaccination.

End point type	Secondary
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End point timeframe:

Prior to (PRE) and one month after (POST) Boostrix vaccination

End point values	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	225	222	223	
Units: Subjects				
Anti-PT, PRE (N=223;222;221)	162	156	153	
Anti-PT, POST (N=225;220;223)	221	220	223	
Anti-FHA, PRE (N=223;222;223)	222	221	220	
Anti-FHA, POST (N=225;220;223)	225	220	223	
Anti-PRN, PRE (N=223;222;221)	200	200	207	
Anti-PRN, POST (N=224;218;221)	223	218	221	

Statistical analyses

No statistical analyses for this end point

Secondary: rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY vaccine response

End point title	rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY vaccine response
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End point description:

rSBA vaccine response for serogroups A, C, W-135 and Y is defined as:

For initially seronegative subjects (pre-vaccination titer below the cut-off of 1:8): number of subjects with rSBA antibody titers \geq 1:32 one month after vaccination.

For initially seropositive subjects (pre-vaccination titer \geq 1:8): number of subjects with rSBA antibody titers at least four times the pre-vaccination antibody titers, one month after vaccination.

End point type	Secondary
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End point timeframe:

At one month after Nimenrix vaccination

End point values	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	226	222	223	
Units: Subjects				
rSBA-MenA (N=225;222;223)	217	207	214	
rSBA-MenC (N=226;222;223)	225	210	215	
rSBA-MenW-135 (N=226;222;223)	225	216	211	
rSBA-MenY (N=226;222;223)	220	214	212	

Statistical analyses

No statistical analyses for this end point

Secondary: Booster responses for anti-PT, anti-FHA and anti-PRN concentrations

End point title	Booster responses for anti-PT, anti-FHA and anti-PRN concentrations
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End point description:

Booster responses to the PT, FHA and PRN antigens, defined as:

For initially seronegative subjects (antibody concentration < 2.046 IU/ml for anti-FHA, concentration < 2.187 IU/ml for anti-

PRN, concentration < 2.693 IU/ml for anti-PT) prior to vaccination: antibody concentration ≥ 4 fold cut-off at one month after the vaccination.

For initially seropositive subjects (antibody concentration ≥ 2.046 IU/ml for anti-FHA, concentration ≥ 2.187 IU/ml for anti-

PRN, concentration ≥ 2.693 IU/ml for anti-PT) prior to vaccination, with pre-vaccination antibody concentration < 4 fold cut-off: antibody concentration ≥ 4 fold the pre-vaccination antibody concentration at one month after the vaccination.

For initially seropositive subjects with pre-vaccination antibody concentration ≥ 4 fold cut-off: antibody concentration ≥ 2 fold the pre-vaccination antibody concentration at one month after the vaccination.

End point type	Secondary
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End point timeframe:

One month after Boostrix vaccination

End point values	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	222	220	223	
Units: Subjects				
Anti-PT (N=222;220;221)	201	188	201	
Anti-FHA (N=222;220;223)	208	210	213	
Anti-PRN (N=221;218;219)	209	198	207	

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 = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 50 millimeters (mm) of injection site.	
End point type	Secondary
End point timeframe:	
During the 4-day (Days 0-3) following each vaccination	

End point values	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	231	228	232	
Units: Subjects				
Any Pain (N=231;228;232)	176	148	167	
Grade 3 Pain (N=231;228;232)	15	19	8	
Any Pain after Boostrix (N=231;225;232)	155	121	156	
Grade 3 Pain after Boostrix (N=231;225;232)	13	12	8	
Any Pain after Nimenrix (N=231;228;232)	121	101	92	
Grade 3 Pain after Nimenrix (N=231;228;232)	7	8	0	
Any Redness (N=231;228;232)	81	75	76	
Grade 3 Redness (N=231;228;232)	4	10	6	
Any Redness after Boostrix (N=231;225;232)	64	56	65	
Grade 3 Redness after Boostrix (N=231;225;232)	3	5	5	
Any Redness after Nimenrix (N=231;228;232)	61	54	39	
Grade 3 Redness after Nimenrix (N=231;228;232)	1	6	4	
Any Swelling (N=231;228;232)	71	71	68	
Grade 3 Swelling (N=231;228;232)	5	9	7	
Any Swelling after Boostrix (N=231;225;232)	57	51	54	
Grade 3 Swelling after Boostrix (N=231;225;232)	3	4	7	

Any Swelling after Nimenrix (N=231;228;232)	48	47	33	
Grade 3 Swelling after Nimenrix (N=231;228;232)	3	5	1	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reporting any, Grade 3 and related general symptoms
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End point description:

Assessed solicited general symptoms were fatigue, gastrointestinal symptoms (nausea, vomiting, diarrhoea and/or abdominal pain), headache and fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.5 °C. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary
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End point timeframe:

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

End point values	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	231	228	232	
Units: Subjects				
Any Fatigue	75	77	81	
Grade 3 Fatigue	2	5	4	
Related Fatigue	70	67	70	
Any Gastrointestinal symptoms	23	31	25	
Grade 3 Gastrointestinal symptoms	2	2	1	
Related Gastrointestinal symptoms	20	25	18	
Any Headache	51	76	65	
Grade 3 Headache	2	5	2	
Related Headache	49	67	53	
Any Fever	14	17	11	
Grade 3 Fever	0	0	0	
Related Fever	10	15	9	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events SAE(s)

End point title	Number of subjects with serious adverse events SAE(s)
End point description: Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life-threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.	
End point type	Secondary
End point timeframe: Throughout the whole study period (from Month 0 up to Month 2)	

End point values	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	231	228	232	
Units: Subjects				
Subjects with any SAEs	0	0	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with new onset of chronic illnesses (NOCIs)

End point title	Number of subjects with new onset of chronic illnesses (NOCIs)
End point description: NOCIs include autoimmune disorders, asthma, type I diabetes, allergies.	
End point type	Secondary
End point timeframe: Throughout the whole study period (from Month 0 up to Month 2)	

End point values	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	231	228	232	
Units: Subjects				
Subjects with any NOCIs	1	5	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events AE(s)

End point title	Number of subjects with unsolicited adverse events AE(s)
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 and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to the vaccination.

End point type	Secondary
End point timeframe:	
Days 0-30 following each vaccination	

End point values	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	231	228	232	
Units: Subjects				
Subjects with any AEs	36	44	58	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Meningitis antibody titers by serum bactericidal assay using rabbit complement (rSBA)

End point title	Anti-Meningitis antibody titers by serum bactericidal assay using rabbit complement (rSBA) ^[13]
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End point description:

The analysis was performed for the serogroups -MenA, -MenC -MenW-135 and -MenY. Antibody titers tabulated as geometric mean titers (GMTs), were obtained by serum bactericidal assay using rabbit complement.

End point type	Secondary
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End point timeframe:

Prior to (PRE) and one month after (POST) Nimenrix vaccination

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Because of splitting into primary/secondary end points for some of the groups, the results were presented separately.

End point values	Boostrix Group			
Subject group type	Reporting group			
Number of subjects analysed	223			
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA, PRE	10.7 (8.5 to 13.4)			
rSBA-MenA, POST	1577.4 (1354.4 to 1837.1)			

rSBA-MenC, PRE	8.3 (6.7 to 10.4)			
rSBA-MenC, POST	1912.6 (1593.9 to 2295.1)			
rSBA-MenW-135, PRE	6.9 (5.6 to 8.5)			
rSBA-MenW-135, POST	3164.6 (2534 to 3952.1)			
rSBA-MenY, PRE	18.2 (13.6 to 24.5)			
rSBA-MenY, POST	4134.4 (3582.3 to 4771.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-D and anti-T concentrations ≥ 1.0 IU/mL

End point title	Number of subjects with anti-D and anti-T concentrations ≥ 1.0 IU/mL ^[14]
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End point description:

The antibody concentrations were calculated as geometric mean concentrations (GMCs) and expressed as international units per milliliter (IU/mL).

End point type	Secondary
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End point timeframe:

At one month after Boostrix vaccination

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Because of splitting into primary/secondary end points for some of the groups, the results were presented separately.

End point values	Nimenrix Group			
Subject group type	Reporting group			
Number of subjects analysed	220			
Units: Subjects				
Anti-D	200			
Anti-T	220			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-D antibody concentrations

End point title	Anti-D antibody concentrations
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End point description:

The antibody concentrations were tabulated as geometric mean concentrations (GMCs) and expressed as international units per milliliter (IU/mL).

End point type	Secondary
End point timeframe:	
Prior to (PRE) and one month after (POST) Boostrix vaccination	

End point values	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	225	220	223	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D, PRE (N=217;220;218)	0.3 (0.3 to 0.4)	0.3 (0.3 to 0.4)	0.3 (0.3 to 0.4)	
Anti-D, POST (N=225;220;223)	4 (3.4 to 4.6)	4.6 (3.9 to 5.4)	4.7 (4 to 5.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-T antibody concentrations

End point title	Anti-T antibody concentrations
End point description:	
The antibody concentrations were tabulated as geometric mean concentrations (GMCs) and expressed as international units per milliliter (IU/mL).	
End point type	Secondary
End point timeframe:	
At Month 0, Month 1 and Month 2	

End point values	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	225	222	223	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-T, Month 0 (N=222;222;223)	0.6 (0.5 to 0.8)	0.6 (0.5 to 0.7)	0.7 (0.5 to 0.8)	
Anti-T, Month 1 (N=225;222;223)	23.5 (20.8 to 26.5)	18.5 (16 to 21.3)	16.3 (14.6 to 18.2)	
Anti-T, Month 2 (N=0;220;223)	0 (0 to 0)	13 (11.7 to 14.5)	13.5 (12.3 to 14.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PT, anti-FHA and anti-PRN antibody concentrations

End point title	Anti-PT, anti-FHA and anti-PRN antibody concentrations ^[15]
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End point description:

The antibody concentrations were tabulated as geometric mean concentrations (GMCs) and expressed as international units per milliliter (IU/mL).

End point type	Secondary
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End point timeframe:

At one month after Boostrix vaccination

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Because of splitting into primary/secondary end points for some of the groups, the results were presented separately.

End point values	Nimenrix Group			
Subject group type	Reporting group			
Number of subjects analysed	220			
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-PT (N=220)	56.7 (49.9 to 64.3)			
Anti-FHA (N=220)	447.3 (403.4 to 496)			
Anti-PRN (N=218)	291.2 (239.1 to 354.6)			

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 (Days 0-3) post-vaccination period; Unsolicited AEs: Days 0-30 following each vaccination; SAEs: throughout the whole study period (from Month 0 up to Month 2).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	Nimenrix+Boostrix Group
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Reporting group description:

Healthy male or female subjects, between and including 11 and 25 years of age, who received one dose of Nimenrix vaccine co-administered with one dose of Boostrix vaccine at Month 0.

Reporting group title	Nimenrix Group
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Reporting group description:

Healthy male or female subjects, between and including 11 and 25 years of age, who received one dose of Nimenrix vaccine at Month 0 and one dose of Boostrix vaccine at Month 1.

Reporting group title	Boostrix Group
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Reporting group description:

Healthy male or female subjects, between and including 11 and 25 years of age, who received one dose of Boostrix vaccine at Month 0 and one dose of Nimenrix vaccine at Month 1.

Serious adverse events	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 231 (0.00%)	0 / 228 (0.00%)	3 / 232 (1.29%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Orthostatic intolerance			
subjects affected / exposed	0 / 231 (0.00%)	0 / 228 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 231 (0.00%)	0 / 228 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			

subjects affected / exposed	0 / 231 (0.00%)	0 / 228 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Nimenrix+Boostrix Group	Nimenrix Group	Boostrix Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	190 / 231 (82.25%)	166 / 228 (72.81%)	180 / 232 (77.59%)
General disorders and administration site conditions			
Pain			
subjects affected / exposed	176 / 231 (76.19%)	148 / 228 (64.91%)	167 / 232 (71.98%)
occurrences (all)	176	222	248
Redness			
subjects affected / exposed	81 / 231 (35.06%)	75 / 228 (32.89%)	76 / 232 (32.76%)
occurrences (all)	81	75	76
Swelling			
subjects affected / exposed	71 / 231 (30.74%)	71 / 228 (31.14%)	68 / 232 (29.31%)
occurrences (all)	71	71	68
Fatigue			
subjects affected / exposed	75 / 231 (32.47%)	77 / 228 (33.77%)	81 / 232 (34.91%)
occurrences (all)	75	77	81
Gastrointestinal symptoms			
subjects affected / exposed	23 / 231 (9.96%)	31 / 228 (13.60%)	25 / 232 (10.78%)
occurrences (all)	23	31	25
Headache			
subjects affected / exposed	51 / 231 (22.08%)	76 / 228 (33.33%)	65 / 232 (28.02%)
occurrences (all)	51	76	65
Fever(Oral)			
subjects affected / exposed	14 / 231 (6.06%)	17 / 228 (7.46%)	11 / 232 (4.74%)
occurrences (all)	14	17	11
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 231 (2.60%)	6 / 228 (2.63%)	12 / 232 (5.17%)
occurrences (all)	6	6	12

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