



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	v1
This version publication date	18 April 2016
First version publication date	06 March 2015

Trial information

Trial identification

Sponsor protocol code	116705
-----------------------	--------

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 for 30 min after vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel.

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	692
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.

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
----------------------------	----------------------------

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
------------------------------	-----

Arm title	Nimenrix™ + Boostrix® Group
------------------	-----------------------------

Arm description:

Subjects received Nimenrix™ co-administered with Boostrix® 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
------------------	-----------------

Arm description:

Subjects received Nimenrix™ at Month 0 and Boostrix® 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 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:	
Subjects received Boostrix® at Month 0 and Nimenrix™ 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, 1 subject in the Nimenrix™ + Boostrix® Group is missing since the subject was enrolled but did not receive any vaccination, hence only 691 subjects started the study.

Baseline characteristics

Reporting groups

Reporting group title	Nimenrix™ + Boostrix® Group
Reporting group description:	
Subjects received Nimenrix™ co-administered with Boostrix® at Month 0.	
Reporting group title	Nimenrix™ Group
Reporting group description:	
Subjects received Nimenrix™ at Month 0 and Boostrix® at Month 1.	
Reporting group title	Boostrix® Group
Reporting group description:	
Subjects received Boostrix® at Month 0 and Nimenrix™ 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			
geometric 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	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: years			
geometric 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: Subjects received Nimenrix™ co-administered with Boostrix® at Month 0.	
Reporting group title	Nimenrix™ Group
Reporting group description: Subjects received Nimenrix™ at Month 0 and Boostrix® at Month 1.	
Reporting group title	Boostrix® Group
Reporting group description: Subjects received Boostrix® at Month 0 and Nimenrix™ at Month 1.	

Primary: rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers

End point title	rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers ^[1]
End point description: At the time of writing this record, data concerning immunogenicity results were not available. The record will be updated when these data become available.	
End point type	Primary
End point timeframe: One month after Nimenrix™ vaccination.	

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: Statistical analyses will be provided if required upon data availability.

End point values	Nimenrix™+ Boostrix® Group	Nimenrix™ Group	Boostrix® Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[2]	0 ^[3]	0 ^[4]	
Units: Titers				
geometric mean (standard deviation)	()	()	()	

Notes:

[2] - Results will be available at a later time.

[3] - Results will be available at a later time.

[4] - Results will be available at a later time.

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[5]
End point description: At the time of writing this record, data concerning immunogenicity results were not available. The record will be updated when these data become available.	
End point type	Primary

End point timeframe:

One month after Boostrix® vaccination.

Notes:

[5] - 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: Statistical analyses will be provided if required upon data availability.

End point values	Nimenrix™ + Boostrix® Group	Nimenrix™ Group	Boostrix® Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[6]	0 ^[7]	0 ^[8]	
Units: Subjects				

Notes:

[6] - Results will be available at a later time

[7] - Results will be available at a later time

[8] - Results will be available at a later time

Statistical analyses

No statistical analyses for this end point

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

End point title	Anti-PT, anti-FHA and anti-PRN antibody concentrations ^[9]
End point description:	
At the time of writing this record, data concerning immunogenicity results were not available. The record will be updated when these data become available.	
End point type	Primary

End point timeframe:

Prior to (i.e. Month 1) and one month after Nimenrix vaccination in the Boostrix Group.

Notes:

[9] - 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: Statistical analyses will be provided if required upon data availability.

End point values	Nimenrix™ + Boostrix® Group	Nimenrix™ Group	Boostrix® Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[10]	0 ^[11]	0 ^[12]	
Units: EU/mL				
median (standard deviation)	()	()	()	

Notes:

[10] - Results will be available at a later time.

[11] - Results will be available at a later time.

[12] - Results will be available at a later time.

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-D and anti-T antibody concentrations

End point title	Anti-D and anti-T antibody concentrations
-----------------	---

End point description:

At the time of writing this record, data concerning immunogenicity results were not available. The record will be updated when these data become available.

End point type	Secondary
----------------	-----------

End point timeframe:

Prior to (i.e. Month 0 for Nimenrix + Boostrix Group and Nimenrix Group and Month 1 for Boostrix Group) and one month after Nimenrix vaccination in all study groups

End point values	Nimenrix™ + Boostrix® Group	Nimenrix™ Group	Boostrix® Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[13]	0 ^[14]	0 ^[15]	
Units: IU/mL				
median (standard deviation)	()	()	()	

Notes:

[13] - Results will be available at a later time.

[14] - Results will be available at a later time.

[15] - Results will be available at a later time.

Statistical analyses

No statistical analyses for this end point

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 $\geq 1:128$
-----------------	---

End point description:

At the time of writing this record, data concerning immunogenicity results were not available. The record will be updated when these data become available.

End point type	Secondary
----------------	-----------

End point timeframe:

Prior to and 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	0 ^[16]	0 ^[17]	0 ^[18]	
Units: Subjects				

Notes:

[16] - Results will be available at a later time

[17] - Results will be available at a later time

[18] - Results will be available at a later time

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-PT, anti-FHA and anti-PRN antibody concentrations ≥ 5.0 EL/mL

End point title	Number of subjects with Anti-PT, anti-FHA and anti-PRN antibody concentrations ≥ 5.0 EL/mL
-----------------	---

End point description:

At the time of writing this record, data concerning immunogenicity results were not available. The record will be updated when these data become available.

End point type	Secondary
----------------	-----------

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	0 ^[19]	0 ^[20]	0 ^[21]	
Units: Subjects				

Notes:

[19] - Results will be available at a later time

[20] - Results will be available at a later time

[21] - Results will be available at a later time

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
-----------------	--

End point description:

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

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

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

At the time of writing this record, data concerning immunogenicity results were not available. The record will be updated when these data become available.

End point type	Secondary
----------------	-----------

End point timeframe:

Prior to (i.e. Month 0 for Nimenrix+Boostrix and Boostrix Groups and Month 1 for Nimenrix group) and 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	0 ^[22]	0 ^[23]	0 ^[24]	
Units: Subjects				

Notes:

[22] - Results will be available at a later time

[23] - Results will be available at a later time

[24] - Results will be available at a later time

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
-----------------	---

End point description:

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

For initially seronegative subjects (pre-vaccination concentration below cut-off: < 5 EU/mL): number of subjects with antibody concentration at least four times the cut-off (post-vaccination concentration ≥ 20 EU/mL).

For initially seropositive subjects with pre-vaccination concentrations ≥ 5 EU/mL and < 20 EU/mL: number of subjects with an increase in antibody concentrations of at least four times the pre-vaccination concentration.

For initially seropositive subjects with pre-vaccination concentrations ≥ 20 EU/mL: number of subjects with an increase in antibody concentrations of at least two times the pre-vaccination concentration.

At the time of writing this record, data concerning immunogenicity results were not available. The record will be updated when these data become available.

End point type	Secondary
----------------	-----------

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	0 ^[25]	0 ^[26]	0 ^[27]	
Units: Subjects				

Notes:

[25] - Results will be available at a later time

[26] - Results will be available at a later time

[27] - Results will be available at a later time

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:

End point type	Secondary
End point timeframe:	
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	229	226	231	
Units: Subjects				
Any Pain after Boostrix	155	121	156	
Any Pain after Nimenrix	121	101	92	
Any Redness after Boostrix	64	56	65	
Any Redness after Nimenrix	61	54	39	
Any Swelling after Boostrix	57	51	54	
Any Swelling after Nimenrix	48	47	33	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting general symptoms

End point title	Number of subjects reporting general symptoms
End point description:	

End point type	Secondary
End point timeframe:	
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	229	226	231	
Units: Subjects				
Any Fatigue	75	77	81	
Any Gastrointestinal symptoms	23	31	25	
Any Headache	51	76	65	
Any Fever (Oral)	14	17	11	

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:

End point type	Secondary
----------------	-----------

End point timeframe:

Throughout the study (Month 0 – 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	0	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with new onset of chronic diseases (NOCIs)
-----------------	---

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

Throughout the study (Month 0 – 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	0	0	0	

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:

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

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: during the 4 days post vaccination

Unsolicited and serious adverse events: up to study end

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	Nimenrix™ + Boostrix® Group
-----------------------	-----------------------------

Reporting group description:

Subjects received Nimenrix™ co-administered with Boostrix® at Month 0.

Reporting group title	Nimenrix™ Group
-----------------------	-----------------

Reporting group description:

Subjects received Nimenrix™ at Month 0 and Boostrix® at Month 1.

Reporting group title	Boostrix® Group
-----------------------	-----------------

Reporting group description:

Subjects received Boostrix® at Month 0 and Nimenrix 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	176 / 231 (76.19%)	148 / 228 (64.91%)	167 / 232 (71.98%)
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	176 / 231 (76.19%)	148 / 228 (64.91%)	167 / 232 (71.98%)
occurrences (all)	176	148	167
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	81 / 231 (35.06%)	75 / 228 (32.89%)	76 / 232 (32.76%)
occurrences (all)	81	75	76
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	71 / 231 (30.74%)	71 / 228 (31.14%)	68 / 232 (29.31%)
occurrences (all)	71	71	68
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	75 / 231 (32.47%)	77 / 228 (33.77%)	81 / 232 (34.91%)
occurrences (all)	75	77	81
Gastrointestinal symptoms			
alternative assessment type: Systematic			
subjects affected / exposed	23 / 231 (9.96%)	31 / 228 (13.60%)	25 / 232 (10.78%)
occurrences (all)	23	31	25
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	51 / 231 (22.08%)	76 / 228 (33.33%)	65 / 232 (28.02%)
occurrences (all)	51	76	65

Fever(Oral) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	14 / 231 (6.06%) 14	17 / 228 (7.46%) 17	11 / 232 (4.74%) 11
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	6 / 231 (2.60%) 6	8 / 228 (3.51%) 8	15 / 232 (6.47%) 15

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