



## Clinical trial results:

**A phase III, open-label, randomised multicentre study to evaluate the immunogenicity and safety of a booster dose of GlaxoSmithKline Biologicals' dTpa-IPV vaccine (Boostrix Polio) compared with Sanofi Pasteur MSD's dTpa-IPV vaccine (Repevax), when co-administered with GSK Biologicals' MMR vaccine (Priorix) in 3 and 4-year-old healthy children.**

### Summary

EudraCT number	2009-012202-39
Trial protocol	GB
Global end of trial date	

### Results information

Result version number	v1
This version publication date	27 April 2016
First version publication date	06 June 2015

### Trial information

#### Trial identification

Sponsor protocol code	111763
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01245049
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, 0044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 0044 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000500-PIP01-08
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	Interim
Date of interim/final analysis	27 March 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 March 2012
Global end of trial reached?	No

Notes:

## General information about the trial

Main objective of the trial:

- To demonstrate that GSK Biologicals' dTpa-IPV vaccine is non-inferior to Sanofi Pasteur MSD's dTpa-IPV vaccine in terms of percentages of subjects with immune response to the diphtheria, tetanus and polio antigens, one month after booster vaccination.
- To demonstrate that GSK Biologicals' dTpa-IPV vaccine given as a single booster dose in this study is non-inferior to GSK Biologicals' DTPa vaccine (Infanrix) given as a primary series in the German household contact study APV-039 in terms of anti-PT, anti-FHA and anti-PRN geometric mean concentrations (GMCs), one month after booster vaccination.

Protection of trial subjects:

The vaccine was administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may have occurred following an intramuscular administration to these subjects. Firm pressure was applied to the injection site (without rubbing) for at least two minutes.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 April 2011
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	United Kingdom: 385
Worldwide total number of subjects	385
EEA total number of subjects	385

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)	385

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

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

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

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Boostrix Polio Group

Arm description:

Subjects received 1 booster dose of Boostrix Polio vaccine co-administered with Priorix

Arm type	Experimental
Investigational medicinal product name	Boostrix Polio
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of Boostrix™ Polio co-administered with Priorix™.

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

Dosage and administration details:

1 dose of Boostrix™ Polio co-administered with Priorix™.

<b>Arm title</b>	Repevax Group
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Arm description:

Subjects received 1 booster dose of Repevax vaccine co-administered with Priorix vaccine

Arm type	Active comparator
Investigational medicinal product name	Repevax™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of Repevax™ Polio co-administered with Priorix™.

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

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Dosage and administration details:

1 dose of Repevax™ co-administered with Priorix™.

<b>Number of subjects in period 1</b>	Boostrix Polio Group	Repevax Group
Started	255	130
Completed	254	126
Not completed	1	4
Consent withdrawn by subject	-	1
Lost to follow-up	-	2
Migrated/moved from study area	-	1
Lost to follow-up	1	-

## Baseline characteristics

### Reporting groups

Reporting group title	Boostrix Polio Group
Reporting group description:	
Subjects received 1 booster dose of Boostrix Polio vaccine co-administered with Priorix	
Reporting group title	Repevax Group
Reporting group description:	
Subjects received 1 booster dose of Repevax vaccine co-administered with Priorix vaccine	

Reporting group values	Boostrix Polio Group	Repevax Group	Total
Number of subjects	255	130	385
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			
arithmetic mean	3.1	3.1	
standard deviation	± 0.25	± 0.24	-
Gender categorical Units: Subjects			
Female	123	65	188
Male	132	65	197

## End points

### End points reporting groups

Reporting group title	Boostrix Polio Group
Reporting group description:	
Subjects received 1 booster dose of Boostrix Polio vaccine co-administered with Priorix	
Reporting group title	Repevax Group
Reporting group description:	
Subjects received 1 booster dose of Repevax vaccine co-administered with Priorix vaccine	

### Primary: Number of subjects with a booster response to diphtheria (D) and tetanus (T) antibodies.

End point title	Number of subjects with a booster response to diphtheria (D) and tetanus (T) antibodies.
End point description:	
Booster response was defined as: for initially seronegative subjects, antibody concentrations at least four times the assay cut-off; for initially seropositive subjects, an increase in antibody concentrations of at least four times the Pre booster vaccination concentration.	
End point type	Primary
End point timeframe:	
One month after booster vaccination	

End point values	Boostrix Polio Group	Repevax Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	90		
Units: Subject				
Anti-D [N=177;90]	176	90		
Anti-T [N=176;90]	173	90		

### Statistical analyses

Statistical analysis title	Non-inferiority in terms of booster response to D
Comparison groups	Boostrix Polio Group v Repevax Group
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[1]</sup>
Method	Standardized asymptotic
Parameter estimate	Percentage difference
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.55
upper limit	3.14

Notes:

[1] - To assess the Non-inferiority of the Boostrix Polio Group compared to the Repevax Group in terms of booster response to diphtheria, standardized asymptotic 95% CI for the groups' difference [Repevax Group minus Boostrix Polio Group] was computed.

Non-inferiority criterion: Upper limit of the 95% CI of the groups' difference in booster response rate  $\leq 10\%$ .

<b>Statistical analysis title</b>	Non-inferiority in terms of booster response to T
Comparison groups	Boostrix Polio Group v Repevax Group
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[2]</sup>
Parameter estimate	Percentage difference
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.43
upper limit	4.9

Notes:

[2] - To assess the Non-inferiority of the Boostrix Polio Group compared to the Repevax Group in terms of booster response to tetanus, standardized asymptotic 95% CI for the groups' difference [Repevax Group minus Boostrix Polio Group] was computed.

Non-inferiority criterion: Upper limit of the 95% CI of the groups' difference in booster response rate  $\leq 10\%$

### **Primary: Concentrations for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN).**

End point title	Concentrations for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN). <sup>[3]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Before (PRE) and one month after (POST) the booster vaccination.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

<b>End point values</b>	Boostrix Polio Group	Repevax Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	96		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-PT PRE [N=171;90]	3.4 (3 to 3.9)	3.2 (2.9 to 3.6)		
Anti-PT POST [N=194;96]	70.1 (62.2 to 79)	47.8 (39.9 to 57.3)		
Anti-FHA PRE [N=174;85]	12.9 (10 to 16.6)	10.7 (7.9 to 14.5)		



Anti-FHA POST [N=195;95]	358.3 (312.5 to 410.8)	164.8 (138.5 to 196.1)		
Anti-PRN PRE [N=175;91]	4.3 (3.8 to 5)	4.3 (3.7 to 5)		
Anti-PRN POST [N=195;94]	151.4 (127.5 to 179.6)	209.8 (168.5 to 261.3)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of seropositive subjects for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN).

End point title	Number of seropositive subjects for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN).
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End point description:

A seropositive subject for anti-PT, anti-FHA and anti-PRN was a subject whose antibody concentration was  $\geq 5$  IU/ml.

End point type	Secondary
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End point timeframe:

Before (PRE) and one month after (POST) the booster vaccination.

End point values	Boostrix Polio Group	Repevax Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	96		
Units: Subject				
Anti-PT PRE [N=171;90]	31	18		
Anti-PT POST [N=194;96]	194	96		
Anti-FHA PRE [N=174;85]	112	60		
Anti-FHA POST [N=195;95]	195	95		
Anti-PRN PRE [N=175;91]	61	37		
Anti-PRN POST [N=195;94]	194	94		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of seroprotected subjects for anti-D and anti-T.

End point title	Number of seroprotected subjects for anti-D and anti-T.
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End point description:

A seroprotected subject was defined a subject with antibody concentrations  $\geq 0.1$  international units per millilitre (IU/mL).

End point type	Secondary
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End point timeframe:

Before (PRE) and one month after (POST) the booster vaccination.

<b>End point values</b>	Boostrix Polio Group	Repevax Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	96		
Units: Subject				
Anti-D PRE [N=177;90]	136	75		
Anti-D POST [N=195;96]	195	96		
Anti-T PRE [N=177;90]	116	63		
Anti-T POST [N=194;96]	194	96		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Concentrations for anti-D and anti-T.

End point title	Concentrations for anti-D and anti-T.
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End point description:

End point type	Secondary
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End point timeframe:

Before (PRE) and one month after (POST) the booster vaccination.

<b>End point values</b>	Boostrix Polio Group	Repevax Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	96		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D PRE [N=177;90]	0.228 (0.194 to 0.267)	0.259 (0.209 to 0.32)		
Anti-D POST [N=195;96]	8.113 (7.259 to 9.068)	11.948 (10.003 to 14.271)		
Anti-T PRE [N=177;90]	0.209 (0.173 to 0.253)	0.241 (0.184 to 0.315)		
Anti-T POST [N=194;96]	6.787 (5.961 to 7.727)	9.194 (7.565 to 11.175)		

### Statistical analyses

No statistical analyses for this end point

**Secondary: Number of seroconverted subjects for anti-measles.**

End point title	Number of seroconverted subjects for anti-measles.
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End point description:

A converted subject was defined an initially seronegative subject with antibody concentrations  $\geq 150$  milli-international units per millilitre (mIU/mL).

End point type	Secondary
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End point timeframe:

Before (PRE) and one month after (POST) the booster vaccination.

End point values	Boostrix Polio Group	Repevax Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: Subject				
Anti-measles PRE [N=4;2]	0	0		
Anti-measles POST [N=4;2]	4	2		

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Concentrations for anti-measles**

End point title	Concentrations for anti-measles
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End point description:

End point type	Secondary
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End point timeframe:

Before (PRE) and one month after (POST) the booster vaccination.

End point values	Boostrix Polio Group	Repevax Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-measles PRE [N=4;2]	75 (75 to 75)	75 (75 to 75)		
Anti-measles POST [N=4;2]	1937.2 (597.6 to 6279.9)	2662.6 (0.9 to 7909745)		

**Statistical analyses**

No statistical analyses for this end point

### Secondary: Number of seroconverted subjects for anti-mumps.

End point title	Number of seroconverted subjects for anti-mumps.
End point description: A converted subject was defined an initially seronegative subject with antibody concentrations $\geq 231$ units per millilitre (U/mL).	
End point type	Secondary
End point timeframe: Before (PRE) and one month after (POST) the booster vaccination.	

End point values	Boostrix Polio Group	Repevax Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	7		
Units: Subjects				
Anti-mumps PRE [N=16;7]	0	0		
Anti-mumps POST [N=11;6]	11	6		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Concentrations for anti-mumps

End point title	Concentrations for anti-mumps
End point description:	
End point type	Secondary
End point timeframe: Before (PRE) and one month after (POST) the booster vaccination.	

End point values	Boostrix Polio Group	Repevax Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	7		
Units: U/mL				
geometric mean (confidence interval 95%)				
Anti-mumps PRE [N=16;7]	115.5 (115.5 to 115.5)	115.5 (115.5 to 115.5)		
Anti-mumps POST [N=11;6]	4131.9 (2453 to 6959.7)	3671.2 (1642.9 to 8203.7)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with a booster response to PT, FHA and PRN antibodies.

End point title	Number of subjects with a booster response to PT, FHA and PRN antibodies.
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End point description:

Booster response was defined as: for initially seronegative subjects, antibody concentrations at least four times the assay cut-off; for initially seropositive subjects, an increase in antibody concentrations of at least four times the Pre booster vaccination concentration.

End point type	Secondary
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End point timeframe:

One month after the booster vaccination.

End point values	Boostrix Polio Group	Repevax Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	90		
Units: Subjects				
Anti-PT [N=170;90]	154	73		
Anti-FHA [N=174;85]	165	79		
Anti-PRN [N= 175;89]	169	89		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with solicited local symptoms.

End point title	Number of subjects with solicited local symptoms.
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End point description:

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) follow-up period after booster vaccination.

End point values	Boostrix Polio Group	Repevax Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	125		
Units: Subjects				
Pain [N=255;125]	134	72		
Redness [N=255;125]	156	77		
Swelling [N=255;125]	99	54		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with solicited general symptoms.

End point title	Number of subjects with solicited general symptoms.
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End point description:

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) follow-up period after booster vaccination.

End point values	Boostrix Polio Group	Repevax Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	125		
Units: Subjects				
Drowsiness [N=255;125]	77	39		
Irritability [N=255;125]	107	49		
Loss of appetite [N=255;125]	67	30		
Temperature [N=255;125]	18	9		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with unsolicited adverse events (AEs).

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

End point type	Secondary
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End point timeframe:

During the 31-day (Days 0-30) follow-up period after booster vaccination.

<b>End point values</b>	Boostrix Polio Group	Repevax Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	130		
Units: Subjects				
AEs [N=255;130]	88	36		

### 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).
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End point description:

End point type	Secondary
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End point timeframe:

During the entire study period.

<b>End point values</b>	Boostrix Polio Group	Repevax Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	130		
Units: Subjects				
SAEs [N=255;130]	1	0		

### 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- (Day 0-Day 3) after vaccination
- Unsolicited adverse events: during the 31 day (Day 0-Day 30) after vaccination
- Serious adverse event from the booster dose up to study end

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.1
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### Reporting groups

Reporting group title	Boostrix Polio Group
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Reporting group description:

Subjects received 1 booster dose of Boostrix Polio vaccine co-administered with Priorix

Reporting group title	Repevax Group
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Reporting group description:

Subjects received 1 booster dose of Repevax vaccine co-administered with Priorix vaccine

Serious adverse events	Boostrix Polio Group	Repevax Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 255 (0.39%)	0 / 130 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Pneumonia			
subjects affected / exposed	1 / 255 (0.39%)	0 / 130 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Boostrix Polio Group	Repevax Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	156 / 255 (61.18%)	77 / 130 (59.23%)	
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			



subjects affected / exposed	134 / 255 (52.55%)	72 / 130 (55.38%)
occurrences (all)	134	72
Redness		
alternative assessment type: Systematic		
subjects affected / exposed	156 / 255 (61.18%)	77 / 130 (59.23%)
occurrences (all)	156	77
Swelling		
subjects affected / exposed	99 / 255 (38.82%)	54 / 130 (41.54%)
occurrences (all)	99	54
Drowsiness		
alternative assessment type: Systematic		
subjects affected / exposed	77 / 255 (30.20%)	39 / 130 (30.00%)
occurrences (all)	77	39
Irritability		
alternative assessment type: Systematic		
subjects affected / exposed	107 / 255 (41.96%)	49 / 130 (37.69%)
occurrences (all)	107	49
Loss of appetite		
alternative assessment type: Systematic		
subjects affected / exposed	67 / 255 (26.27%)	30 / 130 (23.08%)
occurrences (all)	67	30
Temperature/(Axillary)		
alternative assessment type: Systematic		
subjects affected / exposed	18 / 255 (7.06%)	9 / 130 (6.92%)
occurrences (all)	18	9

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported