



## Clinical trial results:

**A phase II, open-label, randomised, multicentre study to evaluate the safety and immunogenicity of GlaxoSmithKline Biologicals' DTPa-HBV-IPV/Hib-MenC-TT vaccine, when given in healthy infants at 3, 5 and 11 months of age.**

### Summary

EudraCT number	2008-006365-91
Trial protocol	SK
Global end of trial date	25 June 2009

### Results information

Result version number	v1
This version publication date	20 November 2018
First version publication date	04 June 2015

### Trial information

#### Trial identification

Sponsor protocol code	111761
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00871741
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com

Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 May 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 May 2009
Global end of trial reached?	Yes
Global end of trial date	25 June 2009
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

- To demonstrate that GSK Biologicals' DTPa-HBV-IPV/Hib-MenC-TT vaccine (Combo group) is non-inferior to GSK Biologicals' DTPa-HBV-IPV/Hib (Infanrix hexa) vaccine co-administered with Novartis' meningococcal serogroup C vaccine (Menjugate) (Control group), in terms of immune response to Hib and MenC antigens, one month after the second vaccine dose.

Criteria for non-inferiority:

Non-inferiority in terms of response to PRP will be demonstrated if the upper limit of the standardized asymptotic 95% confidence interval (CI) on the group difference [Control minus Combo] in percentage of subjects with anti-PRP antibody concentrations  $\geq 0.15 \mu\text{g/ml}$  is  $\leq 10\%$ .

Non-inferiority in terms of response to MenC will be demonstrated if the upper limit of the standardized asymptotic 95% CI on the group difference [Control minus Combo] in percentage of subjects with rSBA-MenC titres  $\geq 8$  is  $\leq 10\%$ .

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination/product administration with appropriate medical treatment readily available. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. Subjects were followed-up for 30 days after the last vaccination/product administration.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 April 2009
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	Slovakia: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	16
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The number of actual participants that completed is 0 (due to study termination no subjects completed the study), however due to a system constraint (0 in an invalid value), the value of 7 and respectively 9 has been entered in the Completed field.

### 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	16
Number of subjects completed	16

### Period 1

Period 1 title	Overall (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>	Combo Group

Arm description:

Subjects in this group were to receive three doses of GSK2202083A vaccine at 3, 5 and 11 months of age.

Arm type	Experimental
Investigational medicinal product name	GSK2202083A vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection in the anterolateral quadrant of the right thigh, three doses at 3, 5 and 11 months of age.

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

Subjects in this group were to receive three doses of Infanrix™ hexa vaccine at 3, 5 and 11 months of age, and two doses of Menjugate vaccine at 3 and 5 months of age.

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

Dosage and administration details:

Intramuscular injection in the left anterolateral thigh, three doses at 3, 5 and 11 months of age.

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

Dosage and administration details:

Intramuscular injection in the right anterolateral thigh, 2 doses at 3 and 5 months of age.

<b>Number of subjects in period 1</b>	Combo Group	Control Group
Started	9	7
Vaccinated	0 <sup>[1]</sup>	0 <sup>[2]</sup>
Completed	9	7

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The study was terminated before the subjects were vaccinated.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The study was terminated before the subjects were vaccinated.

## Baseline characteristics

### Reporting groups

Reporting group title	Combo Group
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Reporting group description:

Subjects in this group were to receive three doses of GSK2202083A vaccine at 3, 5 and 11 months of age.

Reporting group title	Control Group
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Reporting group description:

Subjects in this group were to receive three doses of Infanrix™ hexa vaccine at 3, 5 and 11 months of age, and two doses of Menjugate vaccine at 3 and 5 months of age.

Reporting group values	Combo Group	Control Group	Total
Number of subjects	9	7	16
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: weeks			
arithmetic mean	12.8	13.9	
standard deviation	± 2.28	± 1.57	-
Gender categorical			
Units: Subjects			
Female	2	5	7
Male	7	2	9

## End points

### End points reporting groups

Reporting group title	Combo Group
Reporting group description: Subjects in this group were to receive three doses of GSK2202083A vaccine at 3, 5 and 11 months of age.	
Reporting group title	Control Group
Reporting group description: Subjects in this group were to receive three doses of Infanrix™ hexa vaccine at 3, 5 and 11 months of age, and two doses of Menjugate vaccine at 3 and 5 months of age.	

### Primary: Anti- PRP antibody concentrations $\geq$ 0.15 mg/mL.

End point title	Anti- PRP antibody concentrations $\geq$ 0.15 mg/mL. <sup>[1]</sup>
End point description:	
End point type	Primary
End point timeframe: One Month after the second vaccine dose	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.	

End point values	Combo Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 <sup>[2]</sup>	0 <sup>[3]</sup>		
Units: Subjects				
Anti-PRP				

Notes:  
[2] - As the study was terminated, no blood samples were taken. Hence no immunogenicity analyses were done  
[3] - As the study was terminated, no blood samples were taken. Hence no immunogenicity analyses were done

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any, grade 3 and related solicited local symptoms for Dose 1

End point title	Number of subjects with any, grade 3 and related solicited local symptoms for Dose 1
End point description: The solicited local symptoms assessed were pain, redness and swelling.	
End point type	Secondary
End point timeframe: During the 8-day (Days 0-7) post-vaccination period	

<b>End point values</b>	Combo Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	7		
Units: Subjects				
Any pain	2	2		
Grade 3 pain	0	0		
Any redness	4	4		
Grade 3 redness	0	0		
Any swelling	3	1		
Grade 3 swelling	1	1		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any, grade 3 and related solicited local symptoms for Dose 2.

End point title	Number of subjects with any, grade 3 and related solicited local symptoms for Dose 2. <sup>[4]</sup>
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End point description:

End point type	Secondary
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End point timeframe:

During the 8-day (Days 0-7) post-vaccination period

Notes:

[4] - 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: No subjects from the Control Group had received the second dose of vaccine due to study termination.

<b>End point values</b>	Combo Group			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Subjects				
Any pain	0			
Grade 3 pain	0			
Any redness	0			
Grade 3 redness	0			
Any swelling	0			
Grade 3 swelling	0			

### Statistical analyses

No statistical analyses for this end point

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**Secondary: Number of subjects with any, grade 3 and related solicited local symptoms Across Doses**

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End point title	Number of subjects with any, grade 3 and related solicited local symptoms Across Doses
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End point description:

End point type	Secondary
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End point timeframe:

During the 8-day (Days 0-7) post-vaccination period

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<b>End point values</b>	Combo Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	7		
Units: Subjects				
Any pain	2	2		
Grade 3 pain	0	0		
Any redness	4	4		
Grade 3 redness	0	0		
Any swelling	3	1		
Grade 3 swelling	1	1		

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Number of subjects with any, grade 3 and related solicited general symptoms for Dose 1**

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End point title	Number of subjects with any, grade 3 and related solicited general symptoms for Dose 1
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End point description:

End point type	Secondary
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End point timeframe:

During the 8-day (Days 0-7) post-vaccination period

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<b>End point values</b>	Combo Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	7		
Units: Subjects				
Any drowsiness	1	1		
Grade 3 drowsiness	0	0		

Related drowsiness	1	0		
Any irritability	4	4		
Grade 3 irritability	0	0		
Related irritability	4	3		
Any loss of appetite	2	1		
Grade 3 loss of appetite	0	0		
Related loss of appetite	2	1		
Any temperature	4	1		
>39.0°C	0	0		
Related temperature	4	1		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any, grade 3 and related solicited general symptoms for Dose 2

End point title	Number of subjects with any, grade 3 and related solicited general symptoms for Dose 2 <sup>[5]</sup>
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End point description:

End point type	Secondary
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End point timeframe:

During the 8-day (Days 0-7) post-vaccination period

Notes:

[5] - 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: No subjects from the Control Group had received the second dose of vaccine due to study termination.

End point values	Combo Group			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Subjects				
Any drowsiness	0			
Grade 3 drowsiness	0			
Related drowsiness	0			
Any irritability	0			
Grade 3 irritability	0			
Related irritability	0			
Any loss of appetite	0			
Grade 3 loss of appetite	0			
Related loss of appetite	0			
Any temperature	1			
>39.0°C	0			
Related temperature	1			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any, grade 3 and related solicited general symptoms Across doses

End point title | Number of subjects with any, grade 3 and related solicited general symptoms Across doses

End point description:

End point type | Secondary

End point timeframe:

During the 8-day (Days 0-7) post-vaccination period

End point values	Combo Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	7		
Units: Subjects				
Any drowsiness	1	1		
Grade 3 drowsiness	0	0		
Related drowsiness	1	0		
Any irritability	4	4		
Grade 3 irritability	0	0		
Related irritability	4	3		
Any loss of appetite	2	1		
Grade 3 loss of appetite	0	0		
Related loss of appetite	2	1		
Any temperature >39.0°C	4	1		
Related temperature	0	0		
	4	1		

## 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:

During the 31-day (Days 0-30) post-vaccination period

<b>End point values</b>	Combo Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	7		
Units: Subjects				
Any AE(s)	2	3		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with serious AE(s)

End point title	Number of subjects with serious AE(s)
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End point description:

End point type	Secondary
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End point timeframe:

During the study period

<b>End point values</b>	Combo Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	7		
Units: Subjects				
Any SAE(s)	0	0		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: during the 8-day (Days 0-7) post-vaccination period

AEs: during the 31-day (Days 0-30) post-vaccination period

SAEs: Throughout the entire study period

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	12.0
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### Reporting groups

Reporting group title	Combo Group
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Reporting group description: -

Reporting group title	Control Group
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Reporting group description: -

<b>Serious adverse events</b>	Combo Group	Control Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

<b>Non-serious adverse events</b>	Combo Group	Control Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 9 (44.44%)	4 / 7 (57.14%)	
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 9 (22.22%)	2 / 7 (28.57%)	
occurrences (all)	2	2	
Redness			
alternative assessment type: Systematic			

subjects affected / exposed	4 / 9 (44.44%)	4 / 7 (57.14%)	
occurrences (all)	4	4	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 9 (33.33%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 9 (11.11%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 9 (44.44%)	4 / 7 (57.14%)	
occurrences (all)	4	4	
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 9 (22.22%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Temperature			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 9 (44.44%)	1 / 7 (14.29%)	
occurrences (all)	4	1	
Pyrexia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Rhinitis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Infections and infestations			

Pharyngitis subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 7 (14.29%) 1	
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## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 February 2009	Amendment 1  This protocol amendment is being prepared to allow the analysis of data pertaining to the primary vaccination phase (up to and including Visit 3) as soon as they are available. Additionally the participation of Italy was cancelled before study start hence the protocol has been updated to reflect this. Some bullets related to collection and transcription of diary cards, were misplaced in the list of procedures table which have been corrected.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
26 May 2009	The study was terminated early due to discrepancies between the initial participating countries and the actual participating one. It was deemed that in a single country design there was insufficient justification of using Menjugate® and that the incidence of meningococcal type C disease in children up to 2 years was too low in Slovakia. Following this decision of the Ethics Committee, the study was prematurely terminated after enrolling and vaccinating 16 subjects.	-

Notes:

### Limitations and caveats

None reported