



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	v2 (current)
This version publication date	19 April 2023
First version publication date	04 June 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data set Results have been amended to account for consistency with other registries.

Trial information

Trial identification

Sponsor protocol code	111761
-----------------------	--------

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 greater than or equal to (\geq) 0.15 μ g/ml is lesser than or equal to (\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 ≥ 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
Arm title	GSK2202083A Group

Arm description:

Subjects in this group were to receive three doses of GSK2202083A vaccine at 3, 5 and 11 months of age, as an intramuscular injection in the anterolateral quadrant of the right thigh.

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.

Arm title	Infanrix + Menjugate Group
------------------	----------------------------

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, as an intramuscular injection in the anterolateral quadrant of the right thigh.

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.

Number of subjects in period 1	GSK2202083A Group	Infanrix + Menjugate Group
Started	9	7
Vaccinated	0 ^[1]	0 ^[2]
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 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.

[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 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.

Baseline characteristics

Reporting groups

Reporting group title	GSK2202083A Group
-----------------------	-------------------

Reporting group description:

Subjects in this group were to receive three doses of GSK2202083A vaccine at 3, 5 and 11 months of age, as an intramuscular injection in the anterolateral quadrant of the right thigh.

Reporting group title	Infanrix + Menjugate 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, as an intramuscular injection in the anterolateral quadrant of the right thigh.

Reporting group values	GSK2202083A Group	Infanrix + Menjugate Group	Total
Number of subjects	9	7	16
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	9	7	16
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	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	GSK2202083A Group
Reporting group description: Subjects in this group were to receive three doses of GSK2202083A vaccine at 3, 5 and 11 months of age, as an intramuscular injection in the anterolateral quadrant of the right thigh.	
Reporting group title	Infanrix + Menjugate 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, as an intramuscular injection in the anterolateral quadrant of the right thigh.	

Primary: Anti- PRP antibody concentrations ≥ 0.15 mg/mL

End point title	Anti- PRP antibody concentrations ≥ 0.15 mg/mL ^[1]
End point description: As the study was terminated, no blood samples were taken. Hence no immunogenicity analyses were done.	
End point type	Primary
End point timeframe: At Month 3	

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	GSK2202083A Group	Infanrix + Menjugate Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[2]	0 ^[3]		
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

End point title	Number of subjects with any, grade 3 and related solicited local symptoms
-----------------	---

End point description:

The solicited local symptoms assessed were pain, redness and swelling. Any = any solicited local symptom irrespective of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 20 millimeters (mm) of injection site. Subjects from Control Group did not receive the second study vaccination dose due to study termination.

End point type	Secondary
End point timeframe:	
During the 8-day (Days 0-7) post-vaccination period following each dose and across doses	

End point values	GSK2202083A Group	Infanrix + Menjugate Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	7		
Units: Subjects				
Any pain, Dose 1	2	2		
Grade 3 pain, Dose 1	0	0		
Any redness, Dose 1	4	4		
Grade 3 redness, Dose 1	0	0		
Any swelling, Dose 1	3	1		
Grade 3 swelling, Dose 1	1	1		
Any pain, Dose 2	0	0		
Grade 3 pain, Dose 2	0	0		
Any redness, Dose 2	0	0		
Grade 3 redness, Dose 2	0	0		
Any swelling, Dose 2	0	0		
Grade 3 swelling, Dose 2	0	0		
Any pain, Across doses	2	2		
Grade 3 pain, Across doses	0	0		
Any redness, Across doses	4	4		
Grade 3 redness, Across doses	0	0		
Any swelling, Across doses	3	1		
Grade 3 swelling, Across doses	1	1		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The solicited general symptoms assessed were drowsiness, irritability, loss of appetite and temperature. Any = any general symptom irrespective of intensity grade and relationship to vaccination. Grade 3 Irritability = crying that could not be comforted/prevented normal activity. Grade 3 Drowsiness = drowsiness that prevented normal activity. Grade 3 Loss of Appetite = did not eat at all. Related = symptoms assessed by the investigator as causally related to vaccination. Subjects from Control Group did not receive the second study vaccination dose due to study termination.

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

End point timeframe:

During the 8-day (Days 0-7) post-vaccination period following each dose and across doses

End point values	GSK2202083A Group	Infanrix + Menjugate Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	7		
Units: Subjects				
Any drowsiness, Dose 1	1	1		
Grade 3 drowsiness, Dose 1	0	0		
Related drowsiness, Dose 1	1	0		
Any irritability, Dose 1	4	4		
Grade 3 irritability, Dose 1	0	0		
Related irritability, Dose 1	4	3		
Any loss of appetite, Dose 1	2	1		
Grade 3 loss of appetite, Dose 1	0	0		
Related loss of appetite, Dose 1	2	1		
Any temperature, Dose 1	4	1		
Grade 3 temperature (>39.0°C), Dose 1	0	0		
Related temperature, Dose 1	4	1		
Any drowsiness, Dose 2	0	0		
Grade 3 drowsiness, Dose 2	0	0		
Related drowsiness, Dose 2	0	0		
Any irritability, Dose 2	0	0		
Grade 3 irritability, Dose 2	0	0		
Related irritability, Dose 2	0	0		
Any loss of appetite, Dose 2	0	0		
Grade 3 loss of appetite, Dose 2	0	0		
Related loss of appetite, Dose 2	0	0		
Any temperature, Dose 2	1	0		
Grade 3 temperature (>39.0°C), Dose 2	0	0		
Related temperature, Dose 2	1	0		
Any drowsiness, Across doses	1	1		
Grade 3 drowsiness, Across doses	0	0		
Related drowsiness, Across doses	1	0		
Any irritability, Across doses	4	4		
Grade 3 irritability, Across doses	0	0		
Related irritability, Across doses	4	3		
Any loss of appetite, Across doses	2	1		
Grade 3 loss of appetite, Across doses	0	0		
Related loss of appetite, Across doses	2	1		
Any temperature, Across doses	4	1		
Grade 3 temperature (>39.0°C), Across doses	0	0		
Related temperature, Across doses	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: 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.	
End point type	Secondary
End point timeframe: During the 31-day (Days 0-30) post-vaccination period	

End point values	GSK2202083A Group	Infanrix + Menjugate 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 adverse events (SAEs)

End point title	Number of subjects with serious adverse events (SAEs)
End point description: Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.	
End point type	Secondary
End point timeframe: During the entire study period (from Month 0 to Month 9)	

End point values	GSK2202083A Group	Infanrix + Menjugate 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
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	12.0
--------------------	------

Reporting groups

Reporting group title	Infanrix + Menjugate Group
-----------------------	----------------------------

Reporting group description: -

Reporting group title	GSK2202083A Group
-----------------------	-------------------

Reporting group description: -

Serious adverse events	Infanrix + Menjugate Group	GSK2202083A Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 9 (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 %

Non-serious adverse events	Infanrix + Menjugate Group	GSK2202083A Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 7 (71.43%)	5 / 9 (55.56%)	
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 7 (28.57%)	2 / 9 (22.22%)	
occurrences (all)	2	2	
Redness			
alternative assessment type: Systematic			

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 February 2009	<p>Amendment 1</p> <p>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.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
26 May 2009	<p>The study was terminated early due to discrepancies between the initial participating countries and the actual participating one.</p> <p>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.</p>	-

Notes:

Limitations and caveats

None reported