Clinical trial results:
Persistence of hepatitis B antibodies, immunogenicity and safety of GSK Biologicals' hepatitis B vaccine EngerixTM-B Kinder (SKF103860) challenge dose in adolescents vaccinated with four doses of InfanrixTM hexa (SB217744) during infancy.

Summary

EudraCT number	2013-002821-41
Trial protocol	DE
Global end of trial date	23 September 2014

Results information

Result version number	v1
This version publication date	18 April 2016
First version publication date	10 July 2015

Trial information

Trial identification

Sponsor protocol code	106793

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02052661
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, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 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	Final
Date of interim/final analysis	28 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 September 2014
Global end of trial reached?	Yes
Global end of trial date	23 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the anti-HBs antibody response, in terms of subjects with antibody concentrations >= 100 mIU/ml, to a single challenge dose of HBV vaccine (Engerix-B Kinder) in subjects 12–13 years of age, previously vaccinated with four doses of Infanrix hexa in the first two years of life.

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	13 January 2014
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: 300
Worldwide total number of subjects	300
EEA total number of subjects	300

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)	0
Adolescents (12-17 years)	300
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 Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Engerix™-B Kinder Group

Arm description:

Subjects who were previously primed and boosted with four doses of DTPa-HBV-IPV/Hib in the first two years of life, received a single dose of HBV vaccine.

Arm type	Experimental
Investigational medicinal product name	Engerix™-B Kinder
Investigational medicinal product code	
Other name	HBV vaccine, GlaxoSmithKline (GSK) Biologicals' recombinant hepatitis B vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single dose of HBV vaccine, administered intramuscularly into the deltoid of the non-dominant arm.

Number of subjects in period 1	Engerix™-B Kinder Group
Started	300
Completed	300

Baseline characteristics

Reporting groups	
Reporting group title	Engerix™-B Kinder Group
Reporting group description:	
Subjects who were previously primed and boosted with four doses of DTPa-HBV-IPV/Hib in the first two years of life, received a single dose of HBV vaccine.	

Reporting group values	Engerix™-B Kinder Group	Total	
Number of subjects	300	300	
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	12.3		
standard deviation	± 0.5	-	
Gender categorical Units: Subjects			
Female	150	150	
Male	150	150	

End points

End points reporting groups

Reporting group title	Engerix™-B Kinder Group

Reporting group description:

Subjects who were previously primed and boosted with four doses of DTPa-HBV-IPV/Hib in the first two years of life, received a single dose of HBV vaccine.

Primary: Anti-HBs immune response.

End point title	Anti-HBs immune response.[1]

End point description:

Anti-HBs immune response was defined as the number of subjects with Anti-HBs antibody concentrations ≥ 100 mIU/ml.

End point type	Primary

End point timeframe:

1 month after the single challenge dose of HBV vaccine

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 scope of this primary endpoint was descriptive, no statistical analyses were conducted.

End point values	Engerix™-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	289			
Units: Subjects				
Anti-HBs	272			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody concentrations at 12-13 years of age, after previous vaccination with DTPa-HBV-IPV/Hib.

End point title	Anti-HBs antibody concentrations at 12-13 years of age, after previous vaccination with DTPa-HBV-IPV/Hib.

End point description:

End point type	Secondary

End point timeframe:

Before (PRE) and 1 month after (POST) the single challenge dose of HBV vaccine.

End point values	Engerix™-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	293			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, PRE [N=293]	22.7 (18.5 to 27.9)			
Anti-HBs, POST [N=289]	3502.6 (2672 to 4591.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects anti-HBs antibody concentrations ≥ 6.2 mIU/ml, ≥ 10 mIU/ml, 10 to < 100 mIU/ml and ≥ 100 mIU/ml

End point title	Number of subjects anti-HBs antibody concentrations ≥ 6.2 mIU/ml, ≥ 10 mIU/ml, 10 to < 100 mIU/ml and ≥ 100 mIU/ml

End point description:

End point type	Secondary

End point timeframe:

Before the single challenge dose of HBV vaccine.

End point values	Engerix™-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	293			
Units: Subjects				
Anti-HBs ≥ 6.2 mIU/ml	205			
Anti-HBs ≥ 10 mIU/ml	178			
Anti-HBs 10 to < 100 mIU/ml	116			
Anti-HBs ≥ 100 mIU/ml	62			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects anti-HBs antibody concentrations ≥ 6.2 mIU/ml and ≥ 10 mIU/ml

End point title	Number of subjects anti-HBs antibody concentrations ≥ 6.2 mIU/ml and ≥ 10 mIU/ml

End point description:

End point type	Secondary

End point timeframe:

1 month after the single challenge dose of HBV vaccine.

End point values	Engerix™-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	289			
Units: Subjects				
Anti-HBs ≥ 6.2 mIU/ml	283			
Anti-HBs ≥ 10 mIU/ml	282			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with an anamnestic response to the single challenge dose of HBV vaccine.

End point title	Number of subjects with an anamnestic response to the single challenge dose of HBV vaccine.

End point description:

End point type	Secondary

End point timeframe:

One month after the single challenge dose of HBV vaccine.

End point values	Engerix™-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	287			
Units: Subjects				
Anamnesic response	277			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local symptoms.

End point title	Number of subjects with any solicited local symptoms.

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade.

End point type	Secondary

End point timeframe:

During the 4-day (Day 0–3) follow-up period after the single challenge dose of HBV vaccine.

End point values	Engerix™-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	300			
Units: Subjects				
Pain	132			
Redness	70			
Swelling	29			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general symptoms.

End point title	Number of subjects with any solicited general symptoms.

End point description:

End point type	Secondary

End point timeframe:

During the 4-day (Day 0–3) follow-up period after the single challenge dose of HBV vaccine.

End point values	Engerix™-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	300			
Units: Subjects				
Fatigue	73			
Gastrointestinal	34			
Headache	71			
Temperature/(Axillary)	7			

Statistical analyses

No statistical analyses for this end point

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

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

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 (Day 0–30) follow-up period after the single challenge dose of HBV vaccine.

End point values	Engerix™-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	300			
Units: Subjects				
Any AEs	44			

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

End point values	Engerix™-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	300			
Units: Subjects				
Any SAEs	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: during the 4-day (Day 0–3) follow-up period after vaccination
Unsolicited AEs: during the 31-day (Day 0–30) follow-up period after vaccination
SAEs: During the entire study.

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	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Engerix™-B Kinder Group

Reporting group description:

Subjects who were previously primed and boosted with four doses of DTPa-HBV-IPV/Hib in the first two years of life, received a single dose of HBV vaccine.

Serious adverse events	Engerix™-B Kinder Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 300 (0.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 300 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Forearm fracture			
subjects affected / exposed	1 / 300 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Engerix™-B Kinder Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	132 / 300 (44.00%)		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	132 / 300 (44.00%)		
occurrences (all)	132		
Redness			
subjects affected / exposed	70 / 300 (23.33%)		
occurrences (all)	70		
Swelling			
subjects affected / exposed	29 / 300 (9.67%)		
occurrences (all)	29		
Fatigue			
subjects affected / exposed	73 / 300 (24.33%)		
occurrences (all)	73		
Gastrointestinal			
subjects affected / exposed	34 / 300 (11.33%)		
occurrences (all)	34		
Headache			
subjects affected / exposed	71 / 300 (23.67%)		
occurrences (all)	71		
Temperature/(Axillary)			
subjects affected / exposed	7 / 300 (2.33%)		
occurrences (all)	7		

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