Clinical trial results:
A phase IV, open-label, multicentre study to assess the long-term persistence of antibodies against hepatitis B and the immunogenicity and safety of a challenge dose of hepatitis B vaccine (Engerix-B™ Kinder SKF103860) in children aged 14-15 years, previously primed and boosted in the first two years of life with four doses of GSK Biologicals' DTPa-HBV-IPV/Hib (Infanrix™ hexa SB217744) vaccine.

Summary

EudraCT number	2015-003391-74
Trial protocol	DE
Global end of trial date	05 July 2017

Results information

Result version number	v1 (current)
This version publication date	20 December 2017
First version publication date	20 December 2017

Trial information

Trial identification

Sponsor protocol code	106794

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02798952
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	20 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 July 2017
Global end of trial reached?	Yes
Global end of trial date	05 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immunological response to hepatitis B antigen, in terms of antibody concentrations ≥100 mIU/ml, one month after the single challenge dose of the HBV vaccine in subjects 14-15 years of age, previously vaccinated with four doses of Infanrix hexa in the first two years of life.

Protection of trial subjects:

The subjects will be observed closely for at least 30 minutes following the administration of the vaccine, with appropriate medical treatment readily available in case of anaphylaxis.

Background therapy:

At each study visit, the investigator should question the subject's parent(s)/LAR(s) about any medication/product taken and vaccination received by the subject.

Evidence for comparator: -

Actual start date of recruitment	23 August 2016
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: 302
Worldwide total number of subjects	302
EEA total number of subjects	302

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)	302
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 Infanrix hexa in the first two years of life, received a single challenge dose of Engerix-B Kinder.

Arm type	Experimental
Investigational medicinal product name	Engerix™-B Kinder
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose, intramuscular use

Number of subjects in period 1	Engerix-B Kinder Group
Started	302
Completed	302

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 Infanrix hexa in the first two years of life, received a single challenge dose of Engerix-B Kinder.

Reporting group values	Engerix-B Kinder Group	Total	
Number of subjects	302	302	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	14.4		
standard deviation	± 0.5	-	
Gender categorical Units: Subjects			
Female	142	142	
Male	160	160	
Race/Ethnicity, Customized Units: Subjects			
Asian - South East Asian Heritage	1	1	
Other	1	1	
Asian - Central/South Asian Heritage	1	1	
White - Caucasian / European Heritage	293	293	
African Heritage / African American	2	2	
White - Arabic / North African Heritage	4	4	

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 Infanrix hexa in the first two years of life, received a single challenge dose of Engerix-B Kinder.

Primary: Anti-Hepatitis B surface (anti-HBs) antibody concentrations

End point title	Anti-Hepatitis B surface (anti-HBs) antibody concentrations[1]

End point description:

Concentrations were expressed in geometric mean concentrations (GMCs).

End point type	Primary

End point timeframe:

At Day 30.

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	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	268			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
mIU/mL	1975.7 (1436.1 to 2718.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody concentrations

End point title	Anti-HBs antibody concentrations

End point description:

Concentrations were expressed in geometric mean concentrations (GMCs).

End point type	Secondary

End point timeframe:

At Day 0

End point values	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	268			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
mIU/mL	15.6 (12.8 to 19.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-HBs.

End point title	Number of seropositive subjects for anti-HBs.

End point description:

A seropositve subject was defined as a subject with anti-HBs antibody concentrations above the assay cut-off (≥ 6.2 mIU/ml).

End point type	Secondary

End point timeframe:

At Day 0 and Day 30

End point values	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	268			
Units: Participants				
At Day 0	163			
At Day 30	255			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for anti-HBs.

End point title	Number of seroprotected subjects for anti-HBs.

End point description:

A seroprotected subject was defined as a subject with anti-HBs antibody concentrations equal to or above 10 milli-International units per milliliter (mIU/ml).

End point type	Secondary

End point timeframe:

At Day 0 and day 30

End point values	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	268			
Units: Participants				
At Day 0	144			
At Day 30	250			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-HBs concentrations above the cut-off.

End point title	Number of subjects with anti-HBs concentrations above the cut-off.

End point description:

The cut-off of the assay was ≥ 100 mIU/mL.

End point type	Secondary

End point timeframe:

At Day 0 and Day 30

End point values	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	268			
Units: Participants				
At Day 0	45			
At Day 30	234			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with an anamnestic response to the Hepatitis B challenge dose.

End point title	Number of subjects with an anamnestic response to the Hepatitis B challenge dose.

End point description:

Anamnestic response was defined as: For initially seronegative subjects: antibody concentration ≥10mIU/mL. For initially seropositive subjects: antibody concentration at least four times the pre-challenge antibody concentration.

End point type	Secondary

End point timeframe:

At Day 30

End point values	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	268			
Units: Participants				
Participants	248			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local and general symptoms.

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

End point description:

Solicited local symptoms assessed were pain, redness and swelling at injection site. Solicited general symptoms assessed were fatigue, gastrointestinal symptoms, headache and fever (defined as axillary temperature ≥ 37.5°C).

End point type	Secondary

End point timeframe:

Within 4 days (Day 0 - Day 3) after the vaccination

End point values	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	301			
Units: Participants				
Redness	65			
Pain	101			
Swelling	32			
Fatigue	91			
Gastrointestinal symptoms	33			
Headache	76			
Fever	16			

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)

End point description:

An unsolicited AE was defined as any untoward medical occurrence in a subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

End point type	Secondary

End point timeframe:

Within 31 days (Day 0 - Day 30) after the vaccination.

End point values	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Participants				
Participants	55			

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:

An SAE was defined as any untoward medical occurrence that: resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

From Day 0 to Day 30

End point values	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Participants				
Participants	2			

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 0–3) follow-up period after vaccination. Unsolicited AE(s) and SAE(s): during the entire study period (Days 0-30).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Engerix-B Kinder Group

Reporting group description:

Subjects, who were previously primed and boosted with four doses of Infanrix hexa in the first two years of life, received a single challenge dose of Engerix-B Kinder.

Serious adverse events	Engerix-B Kinder Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 302 (0.66%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	1 / 302 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	1 / 302 (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	197 / 302 (65.23%)		

Nervous system disorders Headache subjects affected / exposed occurrences (all)	 79 / 302 (26.16%) 80		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Injection site erythema subjects affected / exposed occurrences (all) Injection site pain subjects affected / exposed occurrences (all) Injection site swelling subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 91 / 302 (30.13%) 91 65 / 302 (21.52%) 65 101 / 302 (33.44%) 101 32 / 302 (10.60%) 32 16 / 302 (5.30%) 16		
Gastrointestinal disorders Gastrointestinal disorder subjects affected / exposed occurrences (all)	 33 / 302 (10.93%) 33		

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