Clinical trial results:
Immunogenicity and protective efficacy of GlaxoSmithKline Biologicals' rec-Hepatitis B vaccine (10 µg) in newborns of Hepa-titis B envelope antigen positive (HBeAg+) and Hepatitis B surface antigen positive (HBsAg+) mothers compared with a historical control group.

Summary

EudraCT number	2011-002629-23
Trial protocol	Outside EU/EEA
Global end of trial date	25 July 2008

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	08 July 2015

Trial information

Trial identification

Sponsor protocol code	100449

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00240539
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 July 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 July 2008
Global end of trial reached?	Yes
Global end of trial date	25 July 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To evaluate the anti-HBs antibody persistence from Year 16 up to Y 20, after the first vaccine dose of the primary vaccination.
• To evaluate the prevalence and incidence of other hepatitis B markers (HBsAg, anti-HBc, HBeAg, anti-HBe) upto Year 20 after the first vaccine dose of the primary vaccination.
• To evaluate the clinical significance of the HBsAg positive and anti-HBc positive cases observed during the long-term follow-up of this study.

Protection of trial subjects:

Vaccines/products were administered by qualified and trained personnel.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2003
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	Thailand: 36
Worldwide total number of subjects	36
EEA total number of subjects	0

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)	14
Adults (18-64 years)	22
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

Are arms mutually exclusive?	Yes
Arm title	HBsAg(+) & HBeAg(+) 5-dose Group

Arm description:

Newborns of anti-hepatitis B surface antigen positive [HBsAg(+)] and hepatitis B envelope antigen positive [HBeAg(+)] mothers, who received 5 doses of Engerix™ in the primary study.

Arm type	Experimental
Investigational medicinal product name	Engerix™-B Junior
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Four (HBsAg(+) & HBeAg(-) 4-dose Group, HBsAg(+) & HBeAg(+) 4-dose Group and HBsAg(-) & HBeAg(-) 4-dose Group) and five (HBsAg(+) & HBeAg(+) 5-dose Group) doses administered

Arm title	HBsAg(+) & HBeAg(-) 4-dose Group

Arm description:

Newborns of HBsAg(+) and HBeAg negative [HBeAg(-)] mothers, who received 4 doses of Engerix™ in the primary study.

Arm type	Experimental
Investigational medicinal product name	Engerix™-B Junior
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Four (HBsAg(+) & HBeAg(-) 4-dose Group, HBsAg(+) & HBeAg(+) 4-dose Group and HBsAg(-) & HBeAg(-) 4-dose Group) and five (HBsAg(+) & HBeAg(+) 5-dose Group) doses administered

Arm title	HBsAg(-) & HBeAg(-) 4-dose Group

Arm description:

Newborns of HBsAg(-) and HBeAg(-) mothers, who received 4 doses of Engerix™ in the primary study.

Arm type	Experimental

Investigational medicinal product name	Engerix™-B Junior
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Four (HBsAg(+) & HBeAg(-) 4-dose Group, HBsAg(+) & HBeAg(+) 4-dose Group and HBsAg(-) & HBeAg(-) 4-dose Group) and five (HBsAg(+) & HBeAg(+) 5-dose Group) doses administered

Arm title	HBsAg(+) & HBeAg(+) 4-dose Group

Arm description:

Newborns of HBsAg(+) and HBeAg(+) mothers, who received 4 doses of Engerix™ in the primary study.

Arm type	Experimental
Investigational medicinal product name	Engerix™-B Junior
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Four (HBsAg(+) & HBeAg(-) 4-dose Group, HBsAg(+) & HBeAg(+) 4-dose Group and HBsAg(-) & HBeAg(-) 4-dose Group) and five (HBsAg(+) & HBeAg(+) 5-dose Group) doses administered

Number of subjects in period 1	HBsAg(+) & HBeAg(+) 5-dose	HBsAg(+) & HBeAg(-) 4-dose Group	HBsAg(-) & HBeAg(-) 4-dose Group
Started	2	2	1
Completed	2	2	1

Number of subjects in period 1	HBsAg(+) & HBeAg(+) 4-dose
Started	31
Completed	31

Baseline characteristics

Reporting groups	
Reporting group title	HBsAg(+) & HBeAg(+) 5-dose Group
Reporting group description:	
Newborns of anti-hepatitis B surface antigen positive [HBsAg(+)] and hepatitis B envelope antigen positive [HBeAg(+)] mothers, who received 5 doses of Engerix™ in the primary study.	
Reporting group title	HBsAg(+) & HBeAg(-) 4-dose Group
Reporting group description:	
Newborns of HBsAg(+) and HBeAg negative [HBeAg(-)] mothers, who received 4 doses of Engerix™ in the primary study.	
Reporting group title	HBsAg(-) & HBeAg(-) 4-dose Group
Reporting group description:	
Newborns of HBsAg(-) and HBeAg(-) mothers, who received 4 doses of Engerix™ in the primary study.	
Reporting group title	HBsAg(+) & HBeAg(+) 4-dose Group
Reporting group description:	
Newborns of HBsAg(+) and HBeAg(+) mothers, who received 4 doses of Engerix™ in the primary study.	

Reporting group values	HBsAg(+) & HBeAg(+) 5-dose	HBsAg(+) & HBeAg(-) 4-dose Group	HBsAg(-) & HBeAg(-) 4-dose Group
Number of subjects	2	2	1
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	20	19.5	20
standard deviation	± 0	± 0.51	± 0
Gender categorical			
Units: Subjects			
Female	2	2	1
Male	0	0	0

Reporting group values	HBsAg(+) & HBeAg(+) 4-dose	Total	
Number of subjects	31	36	
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	19.5		
standard deviation	± 0.71	-	
Gender categorical			
Units: Subjects			
Female	18	23	
Male	13	13	

End points

End points reporting groups

Reporting group title	HBsAg(+) & HBeAg(+) 5-dose Group
Reporting group description:	
Newborns of anti-hepatitis B surface antigen positive [HBsAg(+)] and hepatitis B envelope antigen positive [HBeAg(+)] mothers, who received 5 doses of Engerix™ in the primary study.	
Reporting group title	HBsAg(+) & HBeAg(-) 4-dose Group
Reporting group description:	
Newborns of HBsAg(+) and HBeAg negative [HBeAg(-)] mothers, who received 4 doses of Engerix™ in the primary study.	
Reporting group title	HBsAg(-) & HBeAg(-) 4-dose Group
Reporting group description:	
Newborns of HBsAg(-) and HBeAg(-) mothers, who received 4 doses of Engerix™ in the primary study.	
Reporting group title	HBsAg(+) & HBeAg(+) 4-dose Group
Reporting group description:	
Newborns of HBsAg(+) and HBeAg(+) mothers, who received 4 doses of Engerix™ in the primary study.	

Primary: Number of subjects seropositive for anti-hepatitis B surface antigen (anti-HBs) antibodies

End point title	Number of subjects seropositive for anti-hepatitis B surface antigen (anti-HBs) antibodies[1][2]
End point description:	
Seropositive subjects are subjects with anti-HBs antibody concentration ≥ 3.3 mIU/mL. This outcome measure applies to HBsAg(+) & HBeAg(+) 5-dose and HBsAg(+) & HBeAg(+) 4-dose Groups only.	
End point type	Primary
End point timeframe:	
At Years 16, 17, 18, 19 and 20 after primary vaccination	

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.
[2] - 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: This outcome measure applies to HBsAg(+) & HBeAg(+) 5-dose and HBsAg(+) & HBeAg (+) 4-dose Groups only.

End point values	HBsAg(+) & HBeAg(+) 5-dose Group	HBsAg(+) & HBeAg(+) 4-dose Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	25		
Units: Subjects				
Year 16 (n= 0, 25)	0	22		
Year 17 (n= 2, 24)	2	21		
Year 18 (n= 1, 22)	1	20		
Year 19 (n= 2, 22)	2	19		
Year 20 (n= 2, 25)	2	23		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects who tested positive for markers of infection with hepatitis B virus

End point title	Number of subjects who tested positive for markers of infection with hepatitis B virus[3][4]

End point description:

Tested markers were hepatitis B surface antigen (HBsAg), antibody to hepatitis B core antigen (anti-HBc), hepatitis B envelope antigen (HBeAg) and antibody to hepatitis B envelope antigen (anti-HBe). This outcome measure applies to HBsAg(+) & HBeAg(+) 5-dose and HBsAg(+) & HBeAg(+) 4-dose Groups only.

End point type	Primary

End point timeframe:

At Years 16, 17, 18, 19 and 20 after primary 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
[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: This outcome measure applies to HBsAg(+) & HBeAg(+) 5-dose and HBsAg(+) & HBeAg (+) 4-dose Groups only.

End point values	HBsAg(+) & HBeAg(+) 5-dose Group	HBsAg(+) & HBeAg(+) 4-dose Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	25		
Units: Subjects				
HBsAg [Year 16] (n= 1, 25)	0	0		
HBsAg [Year 17] (n= 2, 25)	0	1		
HBsAg [Year 18] (n= 1, 22)	0	0		
HBsAg [Year 19] (n= 1, 22)	0	2		
HBsAg [Year 20] (n= 2, 25)	0	2		
Anti-HBc [Year 16] (n= 1, 25)	1	4		
Anti-HBc [Year 17] (n= 2, 25)	1	3		
Anti-HBc [Year 18] (n= 1, 22)	1	2		
Anti-HBc [Year 19] (n= 2, 22)	1	2		
Anti-HBc [Year 20] (n= 2, 25)	1	3		
HBeAg [Year 16] (n= 1, 23)	0	0		
HBeAg [Year 17] (n= 1, 3)	0	0		
HBeAg [Year 18] (n= 1, 2)	0	0		
HBeAg [Year 19] (n= 1, 4)	0	0		
HBeAg [Year 20] (n= 1, 5)	0	0		

Anti-HBe [Year 16] (n= 1, 23)	1	0		
Anti-HBe [Year 17] (n= 1, 4)	1	1		
Anti-HBe [Year 18] (n= 1, 2)	1	0		
Anti-HBe [Year 19] (n= 1, 4)	0	0		
Anti-HBe [Year 20] (n= 1, 5)	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Chronic and With Clinical HBV Infection

End point title	Number of Subjects With Chronic and With Clinical HBV Infection[5]

End point description:

Chronic HBV infection: HBsAg+ and anti-HBc+ at more than 2 consecutive time points.
Clinical HBV infection: Serologically confirmed, symptomatic HBV infection, and all HBV markers negative at consecutive time point.

End point type	Primary

End point timeframe:

From year 16 through to year 20

Notes:

[5] - 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	HBsAg(+) & HBeAg(+) 5-dose Group	HBsAg(+) & HBeAg(-) 4-dose Group	HBsAg(-) & HBeAg(-) 4-dose Group	HBsAg(+) & HBeAg(+) 4-dose Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	1	31
Units: Subjects				
Chronic HBV infection	0	0	0	1
Clinical HBV infection	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
No analysis of safety was performed during this long-term follow-up study.	
Assessment type	Systematic

Dictionary used	
Dictionary name	Not Applicable
Dictionary version	0

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No analysis of safety was performed during this long-term follow-up study.

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