Clinical trial results:
A phase IV, open, multicentric study to evaluate the immune response to a hepatitis B challenge dose in healthy subjects, 72 to 78 months after they received a primary vaccination course of GSK Biologicals' Engerix™-B (thiomersal-free 20 µg or preservative-free 10 µg) vaccine, in the primary study HBV-280.

Summary

EudraCT number	2007-000261-38
Trial protocol	BE
Global end of trial date	14 May 2008

Results information

Result version number	v1
This version publication date	13 May 2016
First version publication date	04 December 2014

Trial information

Trial identification

Sponsor protocol code	108988

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00524576
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 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 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	14 May 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 May 2008
Global end of trial reached?	Yes
Global end of trial date	14 May 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immune response to a challenge dose of hepatitis B vaccine administered in subjects who previously received a complete hepatitis B primary vaccination course, 72 to 78 months ago.

Protection of trial subjects:

As with all injectable vaccines, appropriate medical treatment was always readily available in case of anaphylactic reactions following the administration of the vaccine.
For this reason, the subjects remained under medical supervision for 30 minutes after vaccination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 November 2007
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	Australia: 67
Country: Number of subjects enrolled	Belgium: 77
Worldwide total number of subjects	144
EEA total number of subjects	77

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)	72
Adults (18-64 years)	72
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	Engerix 2 doses + challenge dose

Arm description:

Subjects received 2 doses of Engerix™-B (Month 0 and 6) and a placebo at Month 1 in the primary study and a single dose of Engerix™-B during the booster study.

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

Dosage and administration details:

Subjects received 2 doses of Engerix™-B (Month 0 and 6) and a placebo at Month 1 in the primary study and a single dose of Engerix™-B during the booster study.

Arm title	Engerix 3 doses + challenge dose

Arm description:

Subjects received 3 doses of Engerix™-B (Month 0, 1 and 6) in the primary study and a single dose of Engerix™-B during the booster study.

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

Dosage and administration details:

Subjects received 3 doses of Engerix™-B (Month 0, 1 and 6) in the primary study and a single dose of Engerix™-B during the booster study.

Number of subjects in period 1	Engerix 2 doses + challenge dose	Engerix 3 doses + challenge dose
Started	97	47
Completed	97	47

Baseline characteristics

Reporting groups	
Reporting group title	Engerix 2 doses + challenge dose
Reporting group description:	
Subjects received 2 doses of Engerix™-B (Month 0 and 6) and a placebo at Month 1 in the primary study and a single dose of Engerix™-B during the booster study.	
Reporting group title	Engerix 3 doses + challenge dose
Reporting group description:	
Subjects received 3 doses of Engerix™-B (Month 0, 1 and 6) in the primary study and a single dose of Engerix™-B during the booster study.	

Reporting group values	Engerix 2 doses + challenge dose	Engerix 3 doses + challenge dose	Total
Number of subjects	97	47	144
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	19.3	
standard deviation	± 1.22	± 1.46	-
Gender categorical			
Units: Subjects			
Female	50	23	73
Male	47	24	71

End points

End points reporting groups

Reporting group title	Engerix 2 doses + challenge dose
Reporting group description:	
Subjects received 2 doses of Engerix™-B (Month 0 and 6) and a placebo at Month 1 in the primary study and a single dose of Engerix™-B during the booster study.	
Reporting group title	Engerix 3 doses + challenge dose
Reporting group description:	
Subjects received 3 doses of Engerix™-B (Month 0, 1 and 6) in the primary study and a single dose of Engerix™-B during the booster study.	

Primary: Number of participants with immunological response to challenge dose in terms of anti-hepatitis B surface antigen (anti-HBs) antibody concentration

End point title	Number of participants with immunological response to challenge dose in terms of anti-hepatitis B surface antigen (anti-HBs) antibody concentration[1]
End point description:	
Immune response defined as: *For initially seronegative subjects (anti-HBs antibody concentration <3.3 milli-international unit per milliliter [mIU/mL] before vaccination) antibody concentration ≥ 10mIU/mL at post booster. *For initially seropositive subjects: antibody concentration at post booster ≥ 4-fold the pre-vaccination antibody concentration.	
End point type	Primary
End point timeframe:	
30 days post-challenge 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	Engerix 2 doses + challenge dose	Engerix 3 doses + challenge dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	21		
Units: Subjects				
(anti-HBs) antibody concentration	53	21		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with anti-HBs antibody concentrations above the cut-off value

End point title	Number of participants with anti-HBs antibody concentrations above the cut-off value
End point description:	
Anti-HBs antibody cut-off values assessed include 3.3, 10 and 100 mIU/mL.	
End point type	Secondary

End point timeframe:

30 days post-challenge dose

End point values	Engerix 2 doses + challenge dose	Engerix 3 doses + challenge dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	21		
Units: Subjects				
≥ 3.3 mIU/mL	53	21		
≥ 10 mIU/mL	53	21		
≥ 100 mIU/mL	50	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of anti-HBs antibodies

End point title	Concentration of anti-HBs antibodies

End point description:

Concentrations given as geometric mean concentration (GMC) and expressed in mIU/mL.

End point type	Secondary

End point timeframe:

30 days post-challenge dose

End point values	Engerix 2 doses + challenge dose	Engerix 3 doses + challenge dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	21		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Concentration of anti-HBs antibodies	6214.1 (3213.1 to 12018)	16564.3 (6394.9 to 42905.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants reporting solicited local symptoms

End point title	Number of participants reporting solicited local symptoms

End point description:

Solicited local symptoms assessed include pain, redness and swelling.

End point type	Secondary

End point timeframe:

During the 4-day follow-up period (Day 0-3) after the challenge dose

End point values	Engerix 2 doses + challenge dose	Engerix 3 doses + challenge dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	22		
Units: Subjects				
Pain	22	4		
Redness	11	1		
Swelling	9	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants reporting solicited general symptoms

End point title	Number of participants reporting solicited general symptoms

End point description:

Solicited general symptoms assessed include fatigue, fever, gastrointestinal symptoms, and headache.

End point type	Secondary

End point timeframe:

During the 4-day follow-up period (Day 0-3) after the challenge dose

End point values	Engerix 2 doses + challenge dose	Engerix 3 doses + challenge dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	22		
Units: Subjects				
Fatigue	19	7		
Fever ≥ 37.5 degree Celsius	1	0		
Gastrointestinal disorder	7	4		
Headache	14	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants reporting unsolicited adverse events (AE)

End point title	Number of participants reporting unsolicited adverse events (AE)

End point description:

An AE is 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.

End point type	Secondary

End point timeframe:

During the 31-day follow-up period (Day 0-30) after the challenge dose

End point values	Engerix 2 doses + challenge dose	Engerix 3 doses + challenge dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	22		
Units: Subjects				
Participants reporting AE	19	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants reporting serious adverse events (SAE)

End point title	Number of participants reporting serious adverse events (SAE)

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

End point type	Secondary

End point timeframe:

During the 31-day follow-up period (Day 0-30) after the challenge dose

End point values	Engerix 2 doses + challenge dose	Engerix 3 doses + challenge dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	47		
Units: Subjects				
Participants reporting SAE	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Serious Adverse events (SAE) = Day 0 to Day 30. Solicited local and general symptoms =During the 4-day (Days 0-3) post-challenge dose period. Unsolicited AEs = during the 31-day (Day 0-30) follow-up period after the HBV challenge dose.	
Adverse event reporting additional description:	
For the other adverse events: Data from the Australian center were not included following data quality issues detected at the investigator site.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups	
Reporting group title	Engerix 2 doses + challenge dose
Reporting group description:	
Subjects received 2 doses of Engerix™-B (Month 0 and 6) and a placebo at Month 1 in the primary study and a single dose of Engerix™-B during the booster study.	
Reporting group title	Engerix 3 doses + challenge dose
Reporting group description:	
Subjects received 3 doses of Engerix™-B (Month 0, 1 and 6) in the primary study and a single dose of Engerix™-B during the booster study.	

Serious adverse events	Engerix 2 doses + challenge dose	Engerix 3 doses + challenge dose	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 97 (0.00%)	0 / 47 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Engerix 2 doses + challenge dose	Engerix 3 doses + challenge dose	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 97 (22.68%)	7 / 47 (14.89%)	
Nervous system disorders			
Headache (AE)			
subjects affected / exposed[1]	4 / 55 (7.27%)	2 / 22 (9.09%)	
occurrences (all)	4	2	
General disorders and administration site conditions			

Pain			
alternative assessment type: Systematic			
subjects affected / exposed[2]	22 / 55 (40.00%)	4 / 22 (18.18%)	
occurrences (all)	22	4	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[3]	11 / 55 (20.00%)	1 / 22 (4.55%)	
occurrences (all)	11	1	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[4]	9 / 55 (16.36%)	0 / 22 (0.00%)	
occurrences (all)	9	0	
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed[5]	19 / 55 (34.55%)	7 / 22 (31.82%)	
occurrences (all)	19	7	
Gastrointestinal disorder			
alternative assessment type: Systematic			
subjects affected / exposed[6]	7 / 55 (12.73%)	4 / 22 (18.18%)	
occurrences (all)	7	4	
Headache (Solicited Symptom)			
alternative assessment type: Systematic			
subjects affected / exposed[7]	14 / 55 (25.45%)	4 / 22 (18.18%)	
occurrences (all)	14	4	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects exposed to the adverse event may differ from the total number of subjects exposed for the reporting group as for the unsolicited adverse events, not all subjects reported an event and hence, were considered as subjects without an event.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: For the solicited local and general symptoms, not all subjects had their symptom sheets completed therefore, the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom sheet completed).

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: For the solicited local and general symptoms, not all subjects had their symptom sheets completed therefore, the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom sheet completed).

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: For the solicited local and general symptoms, not all subjects had their symptom sheets

completed therefore, the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom sheet completed).
[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: For the solicited local and general symptoms, not all subjects had their symptom sheets completed therefore, the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom sheet completed).
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: For the solicited local and general symptoms, not all subjects had their symptom sheets completed therefore, the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom sheet completed).
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: For the solicited local and general symptoms, not all subjects had their symptom sheets completed therefore, the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom sheet completed).

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