Clinical trial results:
An Observational Study Evaluating the Long-Term Safety and Immunogenicity of HEPLISAV™ Compared with Engerix-B® in Adults With Chronic Kidney Disease Who Have Previously Received a Hepatitis B Vaccine Series

Summary

EudraCT number	2010-022372-31
Trial protocol	DE
Global end of trial date	09 October 2013

Results information

Result version number	v1 (current)
This version publication date	25 August 2021
First version publication date	25 August 2021
Summary attachment (see zip file)	study-report-dv2-hbv-19 synopsis (study-report-dv2-hbv-19 synopsis.docx)

Trial information

Trial identification

Sponsor protocol code	DV2-HBV-19

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01282762
WHO universal trial number (UTN)	-
Other trial identifiers	US IND Number: BB-IND 12692

Notes:

Sponsors

Sponsor organisation name	Dynavax Technologies Corporation
Sponsor organisation address	2929 Seventh Street, Suite 100 Berkeley, Berkeley, California, United States, 94710
Public contact	Referat Klinische Prüfung, Paul-Ehrlich-Institut (PEI), +49 610377 1811, klinpruefung@pei.de
Scientific contact	Referat Klinische Prüfung, Paul-Ehrlich-Institut (PEI), +49 610377 1811, klinpruefung@pei.de

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	13 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 October 2013
Global end of trial reached?	Yes
Global end of trial date	09 October 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

to evaluate the durability of seroprotection induced by HEPLISAV and Engerix-B as measured by SPR (anti-HBsAg ≥ 10 mIU/mL) at baseline; starting 5 months after the secondary vaccine series; and starting 6 months to 1 year after the first booster dose and 6 months to 1 year after each subsequent booster dose; and starting 6 months after baseline for subjects not requiring a secondary series or booster.

Protection of trial subjects:

All subjects were monitored for safety until study completion. Safety evaluations included assessments of solicited local and systemic post-injection reactions for 7 days following each study injection.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 November 2010
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	United States: 109
Country: Number of subjects enrolled	Canada: 17
Country: Number of subjects enrolled	Germany: 21
Worldwide total number of subjects	147
EEA total number of subjects	21

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)	0
Adults (18-64 years)	72

From 65 to 84 years	75
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 18 centres in the US, 2 centres in Canada and 7 centres in Germany.

Pre-assignment

Screening details:

A total of 147 subjects were enrolled & included in the safety analysis set. Among subjects seroprotected in HBV-17, 9 subjects were removed from the immunogenicity analysis in HBV-19 due to GCP non-compliance. These 9 subjects were seroprotected upon study entry and received no study treatment during HBV-19, therefore there were 138 total subjects

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

NA - observational, long-term follow up study

Arms

Are arms mutually exclusive?	Yes
Arm title	HEPLISAV

Arm description:

HEPLISAV vaccine

Arm type	Experimental
Investigational medicinal product name	HEPLISAV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

20 mcg recombinant HBsAg subtype adw 3000 mcg 1018 ISS adjuvant. Single intramuscular injection (0.5 mL) injected in the deltoid muscle at Month 0.Week 0, Month 1/Week 4 and Month 6/Week 24. Lot numbers TDG010 and TDG013

Arm title	Engerix-B

Arm description:

Engerix-B treatment

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

Dosage and administration details:

20 mcg recombinant HBsAg combined with 500 mcg alum adjuvant. 2 intramuscular injections of 1.0 mL each (for a total dose of 40 mcg BHsAg and 1 mg alum) in the deltoid muscle at Month 0/Week 0, Month 1/Week 4 and Month 6/Week 24. Lot numbers AHBVB910AA and AHBVC111AA (US), AHBVB925AB and AHBVC145AM (Canada) and AHBVB988AB and AHBVC016AC (Germany)

Number of subjects in period 1	HEPLISAV	Engerix-B
Started	73	74
Completed	53	55
Not completed	20	19
Consent withdrawn by subject	4	7
Death	1	2
Other	1	3
Non-GCP Compliance	7	2
Lost to follow-up	7	5

Baseline characteristics

Reporting groups	
Reporting group title	HEPLISAV
Reporting group description:	
HEPLISAV vaccine	
Reporting group title	Engerix-B
Reporting group description:	
Engerix-B treatment	

Reporting group values	HEPLISAV	Engerix-B	Total
Number of subjects	73	74	147
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)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	34	38	72
From 65-84 years	39	36	75
85 years and over	0	0	0
Not Recorded	0	0	0
Age continuous			
Units: years			
arithmetic mean	62.8	60.9	
standard deviation	± 10.44	± 11.26	-
Gender categorical			
Units: Subjects			
Female	22	27	49
Male	51	47	98

Subject analysis sets	
Subject analysis set title	HEPLISAV mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All subjects excluding those with no immunogenicity data who were treated with HEPLISAV	
Subject analysis set title	HEPLISAV Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects enrolled in the study who were treated with HEPLISAV	
Subject analysis set title	Engerix-B mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All subjects excluding those with no immunogenicity data who were treated with Engerix-B	

Subject analysis set title	Engerix-B Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects enrolled in the study who were treated with Engerix-B

Reporting group values	HEPLISAV mITT	HEPLISAV Safety	Engerix-B mITT
Number of subjects	66	73	72
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)		34	
From 65-84 years		39	
85 years and over		0	
Not Recorded		0	
Age continuous Units: years			
arithmetic mean		62.8	
standard deviation	±	± 10.44	±
Gender categorical Units: Subjects			
Female	21	22	45
Male	45	51	27

Reporting group values	Engerix-B Safety		
Number of subjects	74		
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)	38		
From 65-84 years	36		
85 years and over	0		
Not Recorded	0		
Age continuous Units: years			
arithmetic mean	60.9		
standard deviation	± 11.26		

Gender categorical Units: Subjects			
Female	27		
Male	47		

End points

End points reporting groups

Reporting group title	HEPLISAV
Reporting group description: HEPLISAV vaccine	
Reporting group title	Engerix-B
Reporting group description: Engerix-B treatment	
Subject analysis set title	HEPLISAV mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All subjects excluding those with no immunogenicity data who were treated with HEPLISAV	
Subject analysis set title	HEPLISAV Safety
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects enrolled in the study who were treated with HEPLISAV	
Subject analysis set title	Engerix-B mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All subjects excluding those with no immunogenicity data who were treated with Engerix-B	
Subject analysis set title	Engerix-B Safety
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects enrolled in the study who were treated with Engerix-B	

Primary: Seroprotection rate (SPR)

End point title	Seroprotection rate (SPR)[1]

End point description:

SPR defined as the percentage of subjects with anti-HBsAg greater than or equal to 10 mIU/mL.
The comparisons of HEPLISAV and Engerix-B with regards to immunogenicity, and safety endpoints are descriptive. The analyses were performed by seroprotection category and treatment group.
The HBV-19 baseline for the immunogenicity analysis was the last (Week 28) HBV-17 laboratory result for subjects who did not have a scheduled baseline HBV-19 result.

End point type	Primary

End point timeframe:

5 months following the secondary vaccine series.
6 months to 1 year following the first booster dose.
6 months to 1 year following each subsequent booster dose.
6 months after baseline if a secondary series or booster was not required.

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: Desriptive analysis

End point values	HEPLISAV mITT	Engerix-B mITT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	58	61		
Units: Subjects	42	42		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of injections administered during the study

End point title	Number of injections administered during the study

End point description:

End point type	Secondary

End point timeframe:

Overall trial period

End point values	HEPLISAV mITT	Engerix-B mITT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	72		
Units: Number	43	115		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects receiving study injections

End point title	Number of subjects receiving study injections

End point description:

End point type	Secondary

End point timeframe:

Overall trial period

End point values	HEPLISAV mITT	Engerix-B mITT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	73	74		
Units: Number	24	32		

Statistical analyses

No statistical analyses for this end point

Secondary: SPR in subjects with diabetes mellitus

End point title	SPR in subjects with diabetes mellitus

End point description:

End point type	Secondary

End point timeframe:

Baseline, 5 months after secondary vaccine series, 6 months to 1 year after first booster dose, and 6 months to 1 year after each subsequent booster dose

End point values	HEPLISAV mITT	Engerix-B mITT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	31	29		
Units: Number	20	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity (anti-HBsAg greater than or equal to 100 mIU/mL)

End point title	Immunogenicity (anti-HBsAg greater than or equal to 100 mIU/mL)

End point description:

End point type	Secondary

End point timeframe:

Baseline, 5 months after secondary vaccine series, 6 months to 1 year after the first booster dose, and 6 months to 1 year after each subsequent booster dose.

End point values	HEPLISAV mITT	Engerix-B mITT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	47	50		
Units: Number	25	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity measured by anti-HBsAg geometric mean concentrations

End point title	Immunogenicity measured by anti-HBsAg geometric mean concentrations

End point description:

End point type	Secondary

End point timeframe:

Baseline, 5 months after secondary vaccine series, 6 months to 1 year after the first booster dose, and 6 months to 1 year after each subsequent booster dose

End point values	HEPLISAV mITT	Engerix-B mITT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	47	42		
Units: mIU/mL				
geometric mean (confidence interval 95%)	176.8 (107.4 to 297.0)	108.9 (67.1 to 176.7)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Incidence of local and systemic post-injection reactions for 7 days following each study injection

End point title	Incidence of local and systemic post-injection reactions for 7 days following each study injection

End point description:

End point type	Other pre-specified

End point timeframe:

Within 7-days post-injection

End point values	HEPLISAV Safety	Engerix-B Safety		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23	30		
Units: Number	7	6		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Incidence of AEs through 4 weeks following a secondary vaccine series or 4 weeks following a booster injection

End point title	Incidence of AEs through 4 weeks following a secondary vaccine series or 4 weeks following a booster injection

End point description:

End point type	Other pre-specified

End point timeframe:

Overall trial period

End point values	HEPLISAV Safety	Engerix-B Safety		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	32		
Units: Number	4	6		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Incidence of SAEs (German sites) through 6 months after each study injection

End point title	Incidence of SAEs (German sites) through 6 months after each study injection

End point description:

End point type	Other pre-specified

End point timeframe:

Overall trial period

End point values	HEPLISAV Safety	Engerix-B Safety		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	32		
Units: Number	1	1		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Incidence of AESIs

End point title	Incidence of AESIs

End point description:

End point type	Other pre-specified

End point timeframe:

Overall trial period

End point values	HEPLISAV Safety	Engerix-B Safety		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	32		
Units: Number	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All subjects monitored for safety until study completion (48 months). Assessment of solicited local and systemic post injection reactions for 7 days following each injection; AEs and SAEs through 6 months following injection; AESIs until study completion

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14

Reporting groups

Reporting group title	HEPSILAV population receiving at least 1 dose
Reporting group description: -	
Reporting group title	Engerix-B population receiving at least 1 dose

Reporting group description: -

Serious adverse events	HEPSILAV population receiving at least 1 dose	Engerix-B population receiving at least 1 dose	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	1 / 32 (3.13%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasmacytoma			
subjects affected / exposed	0 / 24 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Pneumothorax traumatic			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Epidermolysis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Multi-Organ Failure			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Amyloidosis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	HEPSILAV population receiving at least 1 dose	Engerix-B population receiving at least 1 dose	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 24 (16.67%)	6 / 32 (18.75%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasmacytoma			
subjects affected / exposed	0 / 24 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Pneumothorax traumatic			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Congenital, familial and genetic disorders			
Epidermolysis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Nervous system disorders			

Hypoaesthesia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Neuropathy peripheral			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Oedema			
subjects affected / exposed	2 / 24 (8.33%)	0 / 32 (0.00%)	
occurrences (all)	2	0	
Fatigue			
subjects affected / exposed	0 / 24 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Multi-organ Failure			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Amyloidosis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	

Nausea			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Dyspnoea exertional			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 24 (4.17%)	1 / 32 (3.13%)	
occurrences (all)	1	1	
Muscular weakness			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 24 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Infected bite			
subjects affected / exposed	0 / 24 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	

Upper respiratory tract infection			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Hypercalcaemia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Hypoglycaemia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Metabolic acidosis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 June 2011	Protocol Amendment 1 (Germany)
03 December 2012	Protocol Amendment 2 (Germany)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported