



Clinical trial results:

A Phase 3 Double-Blind Randomized Controlled Trial to Compare the Immunogenicity and Safety of a Three-dose Regimen of Sci-B-Vac™ to a Three-dose Regimen of Engerix-B® in Adults (PROTECT)

Summary

EudraCT number	2017-001819-36
Trial protocol	FI BE
Global end of trial date	08 April 2019

Results information

Result version number	v1 (current)
This version publication date	08 January 2023
First version publication date	08 January 2023

Trial information

Trial identification

Sponsor protocol code	Sci-B-Vac-001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03393754
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	VBI Vaccines
Sponsor organisation address	310 Hunt Club East, Nepean, Canada, K1V 1C1
Public contact	Bebi Yassin-Rajkumar, VBI Vaccines Inc., +1 613749-4200 151, byassin-rajkumar@vbivaccines.com
Scientific contact	Dr Francisco Diaz-Mitoma, VBI Vaccines Inc., +1 613749-4200 151, fdiazmitoma@vbivaccines.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	17 July 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	08 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Co-Primary Objectives of the Trial were:

To demonstrate that the seroprotection rate (SPR) 4 weeks after completion of the three-dose regimen of Sci-B-Vac™ is non-inferior to the SPR 4 weeks after completion of the three-dose regimen of Engerix-B® in adults ≥18 years of old i.e. the lower bound of the 95% two-sided confidence interval (CI) of the difference between the SPR in the Sci-B-Vac™ arm minus the SPR in the Engerix-B® arm, achieved 4 weeks after receiving the third vaccination, will be > - 5%.

and

To demonstrate that the SPR 4 weeks after completion of the three-dose regimen of Sci-B-Vac™ is superior to the SPR 4 weeks after completion of the three-dose regimen of Engerix-B® in older adults ≥ 45 years old i.e. the lower bound of the 95% two-sided CI of the difference between the SPR in the Sci-B-Vac™ arm minus the SPR in the Engerix-B® arm, achieved 4 weeks after receiving the third vaccination, will be > 5%.

Protection of trial subjects:

An independent Data Monitoring Committee (DMC) was established to monitor subject safety. Subjects were provided with a 28-day diary card to record vaccine reactions. Subjects recorded solicited local and systemic AEs on the day of vaccination and for the next 6 days. A safety follow-up telephone call was made 7 days after each vaccination to inquire about local and systemic reactions. Subjects were followed a minimum of 48 weeks after receiving the first vaccination at Study Day 0, with at least a 24 week follow-up safety assessments after receiving the third vaccination.

Background therapy: -

Evidence for comparator:

Engerix-B is approved for active immunization against hepatitis B virus infection (HBV) caused by all known subtypes in non immune subjects.

Actual start date of recruitment	24 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 259
Country: Number of subjects enrolled	United States: 680

Country: Number of subjects enrolled	Belgium: 63
Country: Number of subjects enrolled	Finland: 605
Worldwide total number of subjects	1607
EEA total number of subjects	668

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)	1015
From 65 to 84 years	589
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Participants were recruited through radio and newspaper advertisements.

Pre-assignment

Screening details:

Screening was conducted within 28 days (4 weeks) prior to the first vaccination.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Blinding implementation details:

This was a double-blind study. Both subjects and the study center staff performing outcome measurement were blinded. Randomization and administration of study vaccine was by unblinded qualified health personnel not involved in assessment of outcome measures, whose sole role was to prepare and administer the allocated study vaccine and to perform activities requiring vial handling.

Arms

Are arms mutually exclusive?	Yes
Arm title	Sci-B-Vac®

Arm description:

Sci-B-Vac® (hepatitis B vaccine) Hepatitis B Vaccination, Solution, 10ug, IM injection at Days 0, 28, and 168.

Hepatitis B Vaccination: Prophylactic Hepatitis B Vaccination

Arm type	Experimental
Investigational medicinal product name	Sci-B-Vac®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccination schedule consists of 3 doses (1 mL each) given according to the following schedule: first dose at an elected date; second dose 1 month after the first dose; third dose 6 months after the first dose.

Injected intramuscularly (IM) into the deltoid region.

Arm title	Engerix-B®
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Arm description:

Engerix-B® (hepatitis B vaccine) Hepatitis B Vaccination, Solution, 20ug, IM injection at Days 0, 28, and 168.

Hepatitis B Vaccination: Prophylactic Hepatitis B Vaccination

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:

The vaccination schedule consists of 3 doses (1 mL each) given according to the following schedule: first dose at an elected date; second dose 1 month after the first dose; third dose 6 months after the first dose.

Injected intramuscularly (IM) into the deltoid region.

Number of subjects in period 1	Sci-B-Vac®	Engerix-B®
Started	796	811
Completed	758	785
Not completed	38	26
Adverse event, non-fatal	5	5
Other	30	21
Pregnancy	3	-

Baseline characteristics

Reporting groups

Reporting group title	Sci-B-Vac®
Reporting group description: Sci-B-Vac® (hepatitis B vaccine) Hepatitis B Vaccination, Solution, 10ug, IM injection at Days 0, 28, and 168. Hepatitis B Vaccination: Prophylactic Hepatitis B Vaccination	
Reporting group title	Engerix-B®
Reporting group description: Engerix-B® (hepatitis B vaccine) Hepatitis B Vaccination, Solution, 20ug, IM injection at Days 0, 28, and 168. Hepatitis B Vaccination: Prophylactic Hepatitis B Vaccination	

Reporting group values	Sci-B-Vac®	Engerix-B®	Total
Number of subjects	796	811	1607
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean full range (min-max)	56.6 18 to 86	56.6 18 to 90	-
Gender categorical Units: Subjects			
Female	481	508	989
Male	315	303	618

Subject analysis sets

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects in the All Enrolled Set who received at least 1 vaccination. Subjects were analyzed as vaccinated, ie, a subject was assigned according to the vaccination received. In case of vaccination error, subjects were analyzed as treated.	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description: subjects who received at least 1 injection and had at least baseline and 1 post baseline immunogenicity assessment.	
Subject analysis set title	Per Protocol Set (PPS)
Subject analysis set type	Per protocol
Subject analysis set description: All subjects in the full analysis set who received all 3 injections, had at least baseline and 1 post-baseline immunogenicity assessment (at the time point of interest), were seronegative at baseline, and had no major protocol deviations leading to exclusion.	

Reporting group values	Safety Set	Full Analysis Set (FAS)	Per Protocol Set (PPS)
Number of subjects	1607	1585	1447
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	56.6	56.6	56.8
full range (min-max)	18 to 90	18 to 90	18 to 90
Gender categorical Units: Subjects			
Female	989	975	894
Male	618	610	553

End points

End points reporting groups

Reporting group title	Sci-B-Vac®
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Reporting group description:

Sci-B-Vac® (hepatitis B vaccine) Hepatitis B Vaccination, Solution, 10ug, IM injection at Days 0, 28, and 168.

Hepatitis B Vaccination: Prophylactic Hepatitis B Vaccination

Reporting group title	Engerix-B®
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Reporting group description:

Engerix-B® (hepatitis B vaccine) Hepatitis B Vaccination, Solution, 20ug, IM injection at Days 0, 28, and 168.

Hepatitis B Vaccination: Prophylactic Hepatitis B Vaccination

Subject analysis set title	Safety Set
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Subject analysis set type	Safety analysis
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Subject analysis set description:

All subjects in the All Enrolled Set who received at least 1 vaccination. Subjects were analyzed as vaccinated, ie, a subject was assigned according to the vaccination received. In case of vaccination error, subjects were analyzed as treated.

Subject analysis set title	Full Analysis Set (FAS)
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Subject analysis set type	Full analysis
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Subject analysis set description:

subjects who received at least 1 injection and had at least baseline and 1 post baseline immunogenicity assessment.

Subject analysis set title	Per Protocol Set (PPS)
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Subject analysis set type	Per protocol
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Subject analysis set description:

All subjects in the full analysis set who received all 3 injections, had at least baseline and 1 post-baseline immunogenicity assessment (at the time point of interest), were seronegative at baseline, and had no major protocol deviations leading to exclusion.

Primary: Seroprotection rate (SPR) defined as percentage of adults ≥ 18 years old achieving anti-HBs levels of ≥ 10 mIU/mL in serum at study day 196

End point title	Seroprotection rate (SPR) defined as percentage of adults ≥ 18 years old achieving anti-HBs levels of ≥ 10 mIU/mL in serum at study day 196
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End point description:

To demonstrate that the SPR 4 weeks after completion of the three-dose regimen of Sci-B-Vac® is non-inferior to a three-dose regimen of Engerix-B® in adults ≥ 18 years old; i.e. the lower bound of the 95% two-sided confidence interval (CI) of the difference between the SPR in the Sci-B-Vac® arm minus the SPR in the Engerix-B® arm, achieved 4 weeks after the third vaccination, will be $> -5\%$.

End point type	Primary
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End point timeframe:

Day 196

End point values	Sci-B-Vac®	Engerix-B®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	718	723		
Units: Percentage of Subjects				
number (confidence interval 95%)	91.36 (89.07 to 93.32)	76.49 (73.22 to 79.53)		

Statistical analyses

Statistical analysis title	Co-Primary1
Statistical analysis description:	
Seroprotection rate (SPR) at Study Day 196 in adults ≥ 18 years of age using PPS	
Comparison groups	Sci-B-Vac® v Engerix-B®
Number of subjects included in analysis	1441
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Difference in proportions
Point estimate	14.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.18
upper limit	18.63

Primary: Seroprotection rate (SPR) defined as percentage of adults ≥ 45 years old achieving anti-HBs levels of ≥ 10 mIU/mL in serum at study day 196

End point title	Seroprotection rate (SPR) defined as percentage of adults ≥ 45 years old achieving anti-HBs levels of ≥ 10 mIU/mL in serum at study day 196
End point description:	
To demonstrate that the SPR 4 weeks after completion of the three-dose regimen of Sci-B-Vac® is superior to the SPR 4 weeks after completion of the three-dose regimen of Engerix-B® in older adults ≥ 45 years old i.e. the lower bound of the 95% two-sided CI of the difference between the SPR in the Sci-B-Vac® arm minus the SPR in the Engerix-B® arm, achieved 4 weeks after receiving the third vaccination, will be $> 5\%$.	
End point type	Primary
End point timeframe:	
Day 196	

End point values	Sci-B-Vac®	Engerix-B®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	625	627		
Units: Percentage of Subjects				
number (confidence interval 95%)	89.44 (86.76 to 91.74)	73.05 (69.39 to 76.48)		

Statistical analyses

Statistical analysis title	Co-Primary2
Statistical analysis description:	
Seroprotection rate (SPR) at Study Day 196 in adults ≥ 45 years of age using FAS	
Comparison groups	Sci-B-Vac® v Engerix-B®
Number of subjects included in analysis	1252
Analysis specification	Pre-specified
Analysis type	superiority
Method	Miettinen and Nurminen
Parameter estimate	Difference in proportions
Point estimate	16.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.17
upper limit	20.65

Secondary: Seroprotection rate (SPR) of Sci-B-Vac at study day 168 compared with Engerix-B at study day 196 in adults ≥ 18 years of age

End point title	Seroprotection rate (SPR) of Sci-B-Vac at study day 168 compared with Engerix-B at study day 196 in adults ≥ 18 years of age
End point description:	
To determine whether the SPR after receiving 2 vaccinations of Sci-B-Vac™, evaluated at 4 weeks and 20 weeks after receiving the second vaccination (just prior to receiving the third vaccination), is non-inferior to the SPR 4 weeks after receiving the third vaccination with Engerix-B®	
End point type	Secondary
End point timeframe:	
Sci-B-Vac at Study Day 168 compared with Engerix-B at Study Day 196	

End point values	Sci-B-Vac®	Engerix-B®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	717	723		
Units: Percentage of Subjects				
number (confidence interval 95%)	65.97 (62.37 to 69.44)	76.49 (73.22 to 79.53)		

Statistical analyses

Statistical analysis title	Secondary1
Statistical analysis description:	
Seroprotection rate (SPR) of Sci-B-Vac at Study Day 168 compared with Engerix-B at Day 196 in adults ≥ 18 years of age	
Comparison groups	Sci-B-Vac® v Engerix-B®
Number of subjects included in analysis	1440
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Difference in proportions
Point estimate	-10.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.15
upper limit	-5.86

Secondary: Number of subjects reporting solicited local adverse events day 1 through day 7 after any vaccination

End point title	Number of subjects reporting solicited local adverse events day 1 through day 7 after any vaccination
End point description:	
Analysis of local solicited adverse events with an interval of onset of Day 1 to Day 7 after any vaccination with either Sci-B-Vac® or Engerix-B®, in adults ≥ 18 years old.	
End point type	Secondary
End point timeframe:	
Day of vaccination and 6 subsequent days	

End point values	Sci-B-Vac®	Engerix-B®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	796	811		
Units: number of events	572	379		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited systemic adverse events day 1 through day 7 after any vaccination

End point title	Number of subjects reporting solicited systemic adverse events day 1 through day 7 after any vaccination
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End point description:

Analysis of systemic solicited adverse events with an interval of onset of Day 1 to Day 7 after any vaccination with either Sci-B-Vac® or Engerix-B®, in adults ≥18 years old.

End point type	Secondary
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End point timeframe:

Day of vaccine administration and six subsequent days

End point values	Sci-B-Vac®	Engerix-B®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	796	811		
Units: Number of events	445	396		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events through end of study

End point title	Number of subjects reporting unsolicited adverse events through end of study
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End point description:

Summary of unsolicited treatment-emergent adverse events reported in ≥1% of subjects after vaccination with either Sci-B-Vac® or Engerix-B®, in adults ≥18 years old.

End point type	Secondary
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End point timeframe:

Through end of study (day 336)

End point values	Sci-B-Vac®	Engerix-B®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	796	811		
Units: Number of events	418	441		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events through end of study

End point title	Number of subjects reporting serious adverse events through end of study
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End point description:

Summary of unsolicited serious adverse events reported after vaccination with either Sci-B-Vac® or Engerix-B®, in adults ≥18 years old.

End point type	Secondary
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End point timeframe:

Through end of study (day 336)

End point values	Sci-B-Vac®	Engerix-B®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	796	811		
Units: Number of events	35	27		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

48-week follow-up for serious adverse events (SAEs), medically significant events or new onset of chronic illness (NOCI) (at least 24 weeks after receiving the third vaccination)

Adverse event reporting additional description:

Safety evaluations included standardized methods for local and systemic vaccine reactions, repeated vital signs and physical examinations, medically significant events or new onset of chronic illness (NOCI), and changes in concomitant medications

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	Sci-B-Vac®
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Reporting group description:

Sci-B-Vac® (hepatitis B vaccine) Hepatitis B Vaccination, Solution, 10ug, IM injection at Days 0, 28, and 168.

Hepatitis B Vaccination: Prophylactic Hepatitis B Vaccination

Reporting group title	Engerix-B®
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Reporting group description:

Engerix-B® (hepatitis B vaccine) Hepatitis B Vaccination, Solution, 20ug, IM injection at Days 0, 28, and 168.

Hepatitis B Vaccination: Prophylactic Hepatitis B Vaccination

Serious adverse events	Sci-B-Vac®	Engerix-B®	
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 796 (4.02%)	21 / 811 (2.59%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 796 (0.00%)	2 / 811 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer stage II			

subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Subchorionic haemorrhage			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Troponin increased			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
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			
Ankle fracture			
subjects affected / exposed	1 / 796 (0.13%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back injury			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			

subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (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			
Trisomy 21			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 796 (0.13%)	2 / 811 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	2 / 796 (0.25%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nodal arrhythmia			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 796 (0.13%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peroneal nerve palsy			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis ischaemic			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragmatic hernia			

subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haematoma			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 796 (0.13%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			

subjects affected / exposed	1 / 796 (0.13%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			

subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 796 (0.00%)	1 / 811 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 796 (0.13%)	0 / 811 (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: 5 %

Non-serious adverse events	Sci-B-Vac®	Engerix-B®	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	625 / 796 (78.52%)	526 / 811 (64.86%)	
Nervous system disorders			
Headache	Additional description: Headache events that occurred after 7 days post-vaccination were considered as unsolicited AE		
subjects affected / exposed	274 / 796 (34.42%)	253 / 811 (31.20%)	
occurrences (all)	431	377	
General disorders and administration site conditions			
Fatigue	Additional description: Fatigue events that occurred after 7 days post-vaccination were considered as unsolicited AE		
subjects affected / exposed	242 / 796 (30.40%)	250 / 811 (30.83%)	
occurrences (all)	377	387	

Injection site pain	Additional description: Injection site pain events that occurred after 7 days post-vaccination were considered as unsolicited AE		
	subjects affected / exposed	564 / 796 (70.85%)	364 / 811 (44.88%)
	occurrences (all)	1194	619
Injection site pruritus	Additional description: Injection site pruritus events that occurred after 7 days post-vaccination were considered as unsolicited AE		
	subjects affected / exposed	76 / 796 (9.55%)	66 / 811 (8.14%)
	occurrences (all)	99	84
Gastrointestinal disorders			
	Diarrhoea	Additional description: Diarrhoea events that occurred after 7 days post-vaccination were considered as unsolicited AE	
	subjects affected / exposed	85 / 796 (10.68%)	104 / 811 (12.82%)
	occurrences (all)	111	129
	Nausea	Additional description: Nausea events that occurred after 7 days post-vaccination were considered as unsolicited AE	
	subjects affected / exposed	57 / 796 (7.16%)	77 / 811 (9.49%)
	occurrences (all)	74	94
Musculoskeletal and connective tissue disorders			
	Myalgia	Additional description: Myalgia events that occurred after 7 days post-vaccination were considered as unsolicited AE	
	subjects affected / exposed	283 / 796 (35.55%)	205 / 811 (25.28%)
	occurrences (all)	432	286
Infections and infestations			
	Upper respiratory tract infection		
	subjects affected / exposed	50 / 796 (6.28%)	52 / 811 (6.41%)
	occurrences (all)	56	57

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 July 2017	The overall reason for the amendment is to change the short-term clinical laboratory follow-up on the entire study population to a more intensive clinical laboratory follow up over the full three-dose regimen on a subset (at least 10%) of the entire study population, and to provide per-protocol clarifications in response to study center inquiries.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported