Clinical trial results:
A Hepatitis B Vaccine Challenge Study to Demonstrate the Durability of Protection Against Hepatitis B Virus Infection in Healthy Children Vaccinated Approximately 9 Years Previously With a 2- or 3-Dose Infant Series and Toddler Dose of Vaxelis®

Summary

EudraCT number	2020-000126-26
Trial protocol	FI
Global end of trial date	08 March 2021

Results information

Result version number	v2 (current)
This version publication date	25 September 2021
First version publication date	18 August 2021
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	V419-013

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04490499
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	08 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 December 2020
Global end of trial reached?	Yes
Global end of trial date	08 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to demonstrate the durability of protection against hepatitis B virus (HBV) infection approximately 8-9 years after vaccination with Vaxelis®. This is an estimation study, and no formal hypothesis testing will be performed.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 September 2020
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	Finland: 207
Worldwide total number of subjects	207
EEA total number of subjects	207

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)	207
Adolescents (12-17 years)	0
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:

Approximately 200 planned to be enrolled and 207 were enrolled.

Period 1

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

Arms

Arm title	HBVAXPRO™

Arm description:

Healthy children vaccinated approximately 8-9 years previously with a 2- or 3-dose infant series and toddler dose of Vaxelis® who received a single dose of Hepatitis B vaccine challenge (HBVAXPRO™).

Arm type	Experimental
Investigational medicinal product name	Hepatitis B virus (HBV) vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single 0.5 mL intramuscular dose

Number of subjects in period 1	HBVAXPRO™
Started	207
Vaccinated	205
Completed	205
Not completed	2
Withdrawal By Subject	2

Baseline characteristics

Reporting groups	
Reporting group title	HBVAXPRO™
Reporting group description:	
Healthy children vaccinated approximately 8-9 years previously with a 2- or 3-dose infant series and toddler dose of Vaxelis® who received a single dose of Hepatitis B vaccine challenge (HBVAXPRO™).	

Reporting group values	HBVAXPRO™	Total	
Number of subjects	207	207	
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	8.4		
standard deviation	± 0.5	-	
Gender Categorical Units: Subjects			
Female	97	97	
Male	110	110	
Race Units: Subjects			
Multiple	2	2	
White	205	205	
Ethnicity Units: Subjects			
Hispanic or Latino	2	2	
Not Hispanic or Latino	205	205	

End points

End points reporting groups

Reporting group title	HBVAXPRO™

Reporting group description:

Healthy children vaccinated approximately 8-9 years previously with a 2- or 3-dose infant series and toddler dose of Vaxelis® who received a single dose of Hepatitis B vaccine challenge (HBVAXPRO™).

Primary: Percentage of Participants with a Protective Hepatitis B Surface Antibody Level of ≥10 milli International Units/mL (mIU/mL) at 30 Days Post-Challenge with HBVAXPRO™

End point title	Percentage of Participants with a Protective Hepatitis B Surface Antibody Level of ≥10 milli International Units/mL (mIU/mL) at 30 Days Post-Challenge with HBVAXPRO™[1]

End point description:

Participant serum samples were collected for analysis with an enhanced chemiluminescence (ECi) assay to determine the concentration of antibodies to hepatitis B surface antigen (HBsAg). Response rate was the percentage of participants with a protective hepatitis B surface antibody (anti-HBs) level of ≥ 10 mIU/mL at Day 30 post-challenge. The analysis population consisted of all enrolled participants without deviations from the protocol (i.e., did not receive study vaccine, use of prohibited medicine/vaccine, or blood sample collected outside of analysis window) that may substantially affect the results of the immunogenicity endpoint.

End point type	Primary

End point timeframe:

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: This is a single arm study, and subjects were enrolled in the same vaccination group. Also, this is an estimation study, and no formal hypothesis testing was performed.

End point values	HBVAXPRO™			
Subject group type	Reporting group			
Number of subjects analysed	202			
Units: Percentage of Participants				
number (confidence interval 95%)	99.5 (97.3 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration of Antibodies to Hepatitis B Surface Antigen

End point title	Geometric Mean Concentration of Antibodies to Hepatitis B Surface Antigen

End point description:

Participant serum samples will be assessed with an ECi assay for anti-HBs geometric mean concentrations (GMCs) pre-challenge on Day 1 and 30 days post-challenge with HBVAXPRO™ in mIU/mL. The analysis population consisted of all enrolled participants without deviations from the protocol (i.e., did not receive study vaccine, use of prohibited medicine/vaccine, or blood sample

collected outside of analysis window) that may substantially affect the results of the immunogenicity endpoint.

End point type	Secondary

End point timeframe:

Day 1 and Day 30

End point values	HBVAXPRO™			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Day 1 Pre-challenge (n=205)	9.63 (7.88 to 11.76)			
Day 30 Post-challenge (n=202)	685.84 (605.67 to 776.63)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Up to Day 30

Adverse event reporting additional description:

The analysis population included all participants who received study vaccine and had safety follow-up data after the vaccination. The all cause mortality analysis population included all enrolled participants. Per protocol, reported non-serious adverse events only include non-serious adverse events that lead to study discontinuation.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	HBVAXPRO™

Reporting group description:

Healthy children vaccinated approximately 8-9 years previously with a 2- or 3-dose infant series and toddler dose of Vaxelis® who received a single dose of Hepatitis B vaccine challenge (HBVAXPRO™).

Serious adverse events	HBVAXPRO™		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 205 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	HBVAXPRO™		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 205 (0.00%)		

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: In the vaccinated participant population, no adverse events (AEs) resulting in discontinuation from study were reported.

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