



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 | v1 |
| This version publication date | 18 August 2021 |
| First version publication date | 18 August 2021 |

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 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 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 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 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.

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|----------------------|-----------|
| 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

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|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

Reporting groups

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|-----------------------|-----------|
| Reporting group title | HBVAXPRO™ |
|-----------------------|-----------|

Reporting group description:

Healthy children vaccinated approximately 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