Clinical trial results:
Vaccination Adjuved Against Hepatitis B in SNS Workers Typed as no Responders to Conventional Vaccines.

Summary

EudraCT number	2016-004991-23
Trial protocol	ES
Global end of trial date	31 October 2019

Results information

Result version number	v1 (current)
This version publication date	08 May 2021
First version publication date	08 May 2021
Summary attachment (see zip file)	Summary (IBS-VACANTIB-1701_Results.pdf)

Trial information

Trial identification

Sponsor protocol code	IBS-VACANTIB-1701

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03410953
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IBSAL (INSTITUTO DE INVESTIGACION BIOMEDICA)
Sponsor organisation address	CAU Salamanca. Hospital Virgen de la Vega, 10ª Planta. Paseo de San Vicente, 58-182, Salamanca, Spain, 37007
Public contact	unidad de ensayos clinicos, IBSAL (INSTITUTO DE INVESTIGACION BIOMEDICA), 0034 923210960, ensayosclinicos@ibsal.es
Scientific contact	unidad de ensayos clinicos, IBSAL (INSTITUTO DE INVESTIGACION BIOMEDICA), 0034 923210960, ensayosclinicos@ibsal.es

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	24 February 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To benefit and equip SACYL staff with an additional protection tool against hepatitis B infection.
To evaluate the efficacy of the adjuvanted vaccine in healthy non-responders to conventional hepatitis B vaccine

Protection of trial subjects:

Adequate information of each patient and efficient monitoring of treatment safety through pharmacovigilance.

Background therapy:

Fendrix®, the hepatitis B vaccine formulated with the new AS04 adjuvant (MPL + aluminum salts) by GlaxoSmithKline.

Evidence for comparator: -

Actual start date of recruitment	01 June 2017
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	Spain: 67
Worldwide total number of subjects	67
EEA total number of subjects	67

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)	67
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Health workers with biological risk in their tasks, who have been filed as non-responders to conventional vaccination against Hepatitis B.

Pre-assignment

Screening details:

Anti-HBs antibody titers of <10 mIU/ml following administration of six 20 µg doses of conventional vaccine (two complete series).

Period 1

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

Arms

Arm title	FENDRIX

Arm description:

Fendrix®, the hepatitis B vaccine formulated with the new AS04 adjuvant (MPL + aluminum salts) by GlaxoSmithKline.

Arm type	Experimental
Investigational medicinal product name	Fendrix®
Investigational medicinal product code	650862
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intramuscular use

Dosage and administration details:

4 separate 0.5 ml doses administered at the following schedule: 1 month, 2 months and 6 months from the date of the first dose.

Number of subjects in period 1	FENDRIX
Started	67
Completed	67

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	67	67	
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			
subjects had to work in the SNS —including university students undertaking work placements in SNS health centres (subject to and limited by the specific regulations on health and safety in each autonomous region)— and be of working age.			
Units: years			
median	49.46		
standard deviation	± 11.77	-	
Gender categorical Units: Subjects			
Female	47	47	
Male	20	20	

End points

End points reporting groups

Reporting group title	FENDRIX

Reporting group description:

Fendrix®, the hepatitis B vaccine formulated with the new AS04 adjuvant (MPL + aluminum salts) by GlaxoSmithKline.

Primary: Seroprotection reached

End point title	Seroprotection reached[1]

End point description:

A cumulative analysis of the response data indicated a gradual increase in subjects reaching seroprotection: 68.66% with the first dose, 86.57% with the second dose, 89.55% with the third dose and 94.03% with the fourth dose.

End point type	Primary

End point timeframe:

first dose
second dose
third dose
fourth 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: We only need an descriptive analysis. Of the 67 subjects participating in this trial, 63 (94.03%) attained anti-HBs levels of >10 mIU/ml, indicating seroprotection against HBV. A cumulative analysis of the response data indicated a gradual increase in subjects reaching seroprotection: 68.66% with the first dose, 86.57% with the second dose, 89.55% with the third dose and 94.03% with the fourth dose.

End point values	FENDRIX			
Subject group type	Reporting group			
Number of subjects analysed	67			
Units: 63				
number (not applicable)				
Seroprotected at first dose	46			
Seroprotected at second dose	12			
Seroprotected at third dose	2			
Seroprotected at fourth dose	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

April 13, 2018 and October 31, 2019

Adverse event reporting additional description:

The 67 participants reported 32 adverse effects (AEs), of which 25 were adverse reaction (AR). None of the adverse effects reported were considered serious and all patients recovered from their corresponding adverse effect, suggesting a low risk of serious adverse effects and an acceptable risk in relation to non-serious adverse effects, which corr

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	Vaccinated

Reporting group description:

The 67 participants reported 32 adverse effects (AEs), of which 25 were adverse reaction (AR). None of the adverse effects reported were considered serious and all patients recovered from their corresponding adverse effect, suggesting a low risk of serious adverse effects and an acceptable risk in relation to non-serious adverse effects, which corresponded to those already identified in the Technical Data Sheet.

Serious adverse events	Vaccinated		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 67 (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	Vaccinated		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 67 (31.34%)		
Investigations			
Puncture Zone Pain			
subjects affected / exposed	14 / 67 (20.90%)		
occurrences (all)	19		
Discomfort			
subjects affected / exposed	4 / 67 (5.97%)		
occurrences (all)	4		

Fatigue			
subjects affected / exposed	3 / 67 (4.48%)		
occurrences (all)	3		
Diarrhea			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences (all)	2		
Paresthesia in the puncture area			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences (all)	2		
Cramp			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences (all)	1		
Diverticulitis			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences (all)	1		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

One of the greatest difficulties we encountered while conducting this trial was recruitment, as samples from all hospitals were small. This resulted in the need to extend recruitment to additional centres in order to obtain an optimal study sample.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33334613