Clinical trial results:
A multicenter, randomized, double-blind, active-controlled phase IIb trial as part of the EU-funded UNISEC project to assess the immunogenicity and safety of a BiondVax-developed influenza vaccine (Multimeric-001) followed by an administration of H5N1 influenza vaccine, administered intramuscularly in healthy adults aged 18-60 years.

Summary

EudraCT number	2015-001979-46
Trial protocol	HU
Global end of trial date	12 October 2017

Results information

Result version number	v1 (current)
This version publication date	10 January 2019
First version publication date	10 January 2019
Summary attachment (see zip file)	Summary BVX-007 (summary BVX-007.docx)

Trial information

Trial identification

Sponsor protocol code	BVX-007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02691130
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BiondVax Pharmaceuticals Ltd
Sponsor organisation address	Hadassah Hospital, BJP bldg, Jerusalem, Israel,
Public contact	local representative in Hungary, SanaClis s.r.o., +36 209760341, beata.balati@invitel.hu
Scientific contact	Dr Ben Yedidia, CSO, BiondVax Pharmaceuticals Ltd, +972 89302529, benyedidia@biondvax.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	12 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 September 2016
Global end of trial reached?	Yes
Global end of trial date	12 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the immunogenicity and safety of M-001 in healthy adults.

Protection of trial subjects:

A medical monitor was assigned by the sponsor: Prof. Shai Ashkenazi, M.D. M.sc. at Schneider Children's Medical Center of Israel, who reviewed the MedDRA coding of all adverse events reported during the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 October 2015
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	Hungary: 224
Worldwide total number of subjects	224
EEA total number of subjects	224

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)	224
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

224 healthy participants aged 18-60 years old were assigned to the trial.

Pre-assignment

Screening details:

Inclusion criteria:
-Healthy male or non-pregnant female aged 18-60 years
-Women of childbearing potential and men must agree to practice adequate contraception
- Is in good health
- Able to understand and comply with study procedures
-signs informed consent

Pre-assignment period milestones

Number of subjects started	224
Number of subjects completed	224

Period 1

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

Blinding implementation details:

The study is double-blinded. To maintain blinding, the preparation of the IMP and control was performed by an unblinded Qualified Person other than the person giving the injection since the prepared IMP and control (saline) differ in appearance. The syringe content was hidden by a label, including the necessary trial randomization information. Only the unblinded study pharmacist/prepared the dosing and used the study randomization code to assign each subject to the appropriate treatment group

Arms

Are arms mutually exclusive?	Yes
Arm title	M-001 High

Arm description:

2 administrations of M-001 at a dose of 1mg, experimental treatment group

Arm type	Experimental
Investigational medicinal product name	M-001
Investigational medicinal product code	
Other name	Multimeric-001
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5mg (Low) or 1.0mg (High) per dose

Arm title	M-001 Low

Arm description:

2 administrations of M-001 at a dose of 0.5mg, experimental treatment group

Arm type	Experimental

Investigational medicinal product name	M-001
Investigational medicinal product code	
Other name	Multimeric-001
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:
0.5mg per dose

Arm title	Placebo

Arm description:
Saline Placebo

Arm type	Placebo
Investigational medicinal product name	saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:
0.5mL per IM injection

Number of subjects in period 1	M-001 High	M-001 Low	Placebo
Started	74	75	75
Completed	74	75	75

Baseline characteristics

Reporting groups	
Reporting group title	M-001 High
Reporting group description:	
2 administrations of M-001 at a dose of 1mg, experimental treatment group	
Reporting group title	M-001 Low
Reporting group description:	
2 administrations of M-001 at a dose of 0.5mg, experimental treatment group	
Reporting group title	Placebo
Reporting group description:	
Saline Placebo	

Reporting group values	M-001 High	M-001 Low	Placebo
Number of subjects	74	75	75
Age categorical			
18-60 years old			
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)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
18-60	74	75	75
Gender categorical			
Units: Subjects			
Female	51	47	46
Male	23	28	29

Reporting group values	Total		
Number of subjects	224		
Age categorical			
18-60 years old			
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		
18-60	224		

Gender categorical Units: Subjects			
Female	144		
Male	80		

Subject analysis sets

Subject analysis set title	High Dose
Subject analysis set type	Full analysis
Subject analysis set description: All the subjects were analyzed for all endpoints	
Subject analysis set title	Low Dose
Subject analysis set type	Full analysis
Subject analysis set description: All the subjects were analyzed for all endpoints	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: All the subjects were analyzed for all endpoints	

Reporting group values	High Dose	Low Dose	Placebo
Number of subjects	74	75	75
Age categorical			
18-60 years old			
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)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
18-60	74	75	75
Gender categorical Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	M-001 High
Reporting group description:	
2 administrations of M-001 at a dose of 1mg, experimental treatment group	
Reporting group title	M-001 Low
Reporting group description:	
2 administrations of M-001 at a dose of 0.5mg, experimental treatment group	
Reporting group title	Placebo
Reporting group description:	
Saline Placebo	
Subject analysis set title	High Dose
Subject analysis set type	Full analysis
Subject analysis set description:	
All the subjects were analyzed for all endpoints	
Subject analysis set title	Low Dose
Subject analysis set type	Full analysis
Subject analysis set description:	
All the subjects were analyzed for all endpoints	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
All the subjects were analyzed for all endpoints	

Primary: safety

End point title	safety
End point description:	
To evaluate the number of participants with related solicited AEs in all subjects until 21 days after the last dosing of the study vaccine (M-001)	
End point type	Primary
End point timeframe:	
Day 0-42	

End point values	M-001 High	M-001 Low	Placebo	High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	74	75	75	74
Units: Number and severity of adverse events	74	75	75	74

End point values	Low Dose	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	75	75		
Units: Number and severity of adverse events	75	75		

Statistical analyses

Statistical analysis title	Safety in treatment vs control group
Comparison groups	M-001 High v M-001 Low v Placebo
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA

Primary: Immunogenicity

End point title	Immunogenicity

End point description:

To evaluate the absolute proportions of responders with CD4+ T cells that produce any Th1 cytokines based on multiparametric FACS analysis in all groups on day 0 and 42

End point type	Primary

End point timeframe:

0-42

End point values	M-001 High	M-001 Low	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74	75	75	
Units: % responders	74	75	75	

Statistical analyses

Statistical analysis title	% responders with CD4+ TH1 response

Statistical analysis description:

Absolute proportions of responders with CD4+ T cells that produce any Th1 cytokines after 2 immunizations in the experimental and control groups.

Comparison groups	M-001 High v M-001 Low v Placebo
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Chi-squared

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 180 days post second immunization	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	High Dose
Reporting group description: -	
Reporting group title	Low Dose
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	High Dose	Low Dose	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 74 (1.35%)	0 / 75 (0.00%)	1 / 75 (1.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Reproductive system and breast disorders			
Vaginal prolapse	Additional description: Unrelated to treatment		
subjects affected / exposed	0 / 74 (0.00%)	0 / 75 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 74 (1.35%)	0 / 75 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0.5 %

Non-serious adverse events	High Dose	Low Dose	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 74 (6.76%)	2 / 75 (2.67%)	4 / 75 (5.33%)
General disorders and administration site conditions			
Pain of skin	Additional description: Mild severity of pain in the administration site immediately after IM injection that is definitely related to the treatment		
subjects affected / exposed	2 / 74 (2.70%)	1 / 75 (1.33%)	1 / 75 (1.33%)
occurrences (all)	2	1	1
Erythema	Additional description: Mild Erythema that is definitely related to the treatment		
subjects affected / exposed	0 / 74 (0.00%)	0 / 75 (0.00%)	2 / 75 (2.67%)
occurrences (all)	0	0	2
Induration	Additional description: Moderate induration that is definitely related to the treatment		
subjects affected / exposed	1 / 74 (1.35%)	0 / 75 (0.00%)	1 / 75 (1.33%)
occurrences (all)	1	0	1
Swelling	Additional description: Mild swelling that is definitely related to the treatment		
subjects affected / exposed	1 / 74 (1.35%)	1 / 75 (1.33%)	0 / 75 (0.00%)
occurrences (all)	1	1	0
warmth	Additional description: Mild warmth that is definitely related to the treatment		
subjects affected / exposed	1 / 74 (1.35%)	0 / 75 (0.00%)	0 / 75 (0.00%)
occurrences (all)	1	0	0

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