Clinical trial results:
A Phase 4, Single-Arm, Open-Label Study Describing The Safety And Immunogenicity of Bexsero in Healthy Subjects Aged 12 Years to Less Than (<) 19 Years

Summary

EudraCT number	2014-003822-42
Trial protocol	DK
Global end of trial date	20 January 2016

Results information

Result version number	v1 (current)
This version publication date	13 August 2016
First version publication date	13 August 2016

Trial information

Trial identification

Sponsor protocol code	B1971048

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Pfizer ClinicalTrials.gov Call Center
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer, Inc., Pfizer ClinicalTrials.gov Call Center, 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer, Inc., Pfizer ClinicalTrials.gov Call Center, 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.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	27 April 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the immune response, relative to baseline status, following receipt of Bexsero as measured by serum bactericidal assay using human complement (hSBA) performed with a panel of Neisseria meningitidis serogroup B (MnB) test strains assessed 1 month after the second vaccination with Bexsero vaccine.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 March 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	Denmark: 71
Worldwide total number of subjects	71
EEA total number of subjects	71

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)	62
Adults (18-64 years)	9
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 71 subjects were enrolled in this study. Of these, 68 subjects received study vaccination.

Period 1

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

Arms

Arm title	Bexsero

Arm description:

Subjects received at least 1 vaccination of Bexsero at Month 0,-2 visits.

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	Neisseria meningitidis serogroup B bivalent recombinant lipoprotein 2086 vaccine (rLP2086)
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Bexsero was administered intramuscularly by injecting 0.5 milliliter (mL) into the upper deltoid muscle at Visit 1 (Month 0) and Visit 2 (Month 2).

Number of subjects in period 1	Bexsero
Started	71
Completed	65
Not completed	6
Consent withdrawn by subject	1
Did not meet entrance criteria	1
Adverse event	3
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Bexsero
Reporting group description:	
Subjects received at least 1 vaccination of Bexsero at Month 0,-2 visits.	

Reporting group values	Bexsero	Total	
Number of subjects	71	71	
Age Categorical Units: Subjects			
12- <15 years	34	34	
15 - <19 years	37	37	
Age Continuous Units: years			
arithmetic mean	14.8		
standard deviation	± 1.93	-	
Gender Categorical Units: Subjects			
Female	34	34	
Male	37	37	

End points

End points reporting groups

Reporting group title	Bexsero

Reporting group description:

Subjects received at least 1 vaccination of Bexsero at Month 0,-2 visits.

Primary: Percentage of Subjects With 4-Fold Rise in Serum Bactericidal Assay Using Human Complement (hSBA) Titer Level

End point title	Percentage of Subjects With 4-Fold Rise in Serum Bactericidal Assay Using Human Complement (hSBA) Titer Level[1]

End point description:

Immunogenicity was assessed in terms of percentage of subjects achieving 4-fold rise on the serotype-specific antibody titer from pre vaccination (Day 1) to 1 month post Vaccination 2, for each of the 4 primary MnB test strains. Evaluable immunogenicity population included eligible subjects who received scheduled investigational product, had pre and post Vaccination 2 blood drawn at pre-specified time points, had valid and determinate assay results for the proposed analysis, received no prohibited vaccines and had no other major protocol deviations. Here, 'n' signifies evaluable subjects included in analysis for the given strain.

End point type	Primary

End point timeframe:

1 month after Vaccination 2

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: Only descriptive data was planned to be reported for this endpoint.

End point values	Bexsero			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: Percentage of subjects				
number (confidence interval 95%)				
Strain 1 (n =61)	91.8 (81.9 to 97.3)			
Strain 2 (n =63)	73 (60.3 to 83.4)			
Strain 3 (n =59)	37.3 (25 to 50.9)			
Strain 4 (n =56)	37.5 (24.9 to 51.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 1

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 1[2]

End point description:

Local reactions were reported using an electronic diary. Pain was scaled as any (any pain at injection site); mild (did not interfere with activity); moderate (interfered with activity); severe (prevented daily activity). Redness and swelling were scaled as any (greater than or equal to [>=] 2.5 centimeters [cm]); mild (2.5 cm to 5.0 cm); moderate (5.5 cm to 10.0 cm); severe (greater than [>] 10.0 cm). Vaccination 1 safety population included all subjects who received at least 1 dose of Bexsero vaccine and had safety information available from Vaccination 1 until prior to Vaccination 2.

End point type	Primary

End point timeframe:

Within 7 days after Vaccination 1

Notes:

[2] - 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: Only descriptive data was planned to be reported for this endpoint.

End point values	Bexsero			
Subject group type	Reporting group			
Number of subjects analysed	68			
Units: Percentage of subjects				
number (confidence interval 95%)				
Pain at injection site: Any	94.1 (85.6 to 98.4)			
Pain at injection site: Mild	26.5 (16.5 to 38.6)			
Pain at injection site: Moderate	58.8 (46.2 to 70.6)			
Pain at injection site: Severe	8.8 (3.3 to 18.2)			
Redness: Any	11.8 (5.2 to 21.9)			
Redness: Mild	7.4 (2.4 to 16.3)			
Redness: Moderate	4.4 (0.9 to 12.4)			
Redness: Severe	0 (0 to 5.3)			
Swelling: Any	14.7 (7.3 to 25.4)			
Swelling: Mild	7.4 (2.4 to 16.3)			
Swelling: Moderate	7.4 (2.4 to 16.3)			
Swelling: Severe	0 (0 to 5.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 2

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 2[3]

End point description:

Local reactions were reported using an electronic diary. Pain was scaled as any (any pain at injection site); mild (did not interfere with activity); moderate (interfered with activity); severe (prevented daily activity). Redness and swelling were scaled as any (>=2.5 cm); mild (2.5 cm to 5.0 cm); moderate (5.5

cm to 10.0 cm); severe (>10.0 cm). Vaccination 2 safety population included all subjects who received at least 1 dose of Bexsero vaccine and had safety information available from Vaccination 2 to post Vaccination 2 blood drawn.

End point type	Primary

End point timeframe:

Within 7 days after Vaccination 2

Notes:

[3] - 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: Only descriptive data was planned to be reported for this endpoint.

End point values	Bexsero			
Subject group type	Reporting group			
Number of subjects analysed	66			
Units: Percentage of subjects				
number (confidence interval 95%)				
Pain at injection site: Any	87.9 (77.5 to 94.6)			
Pain at injection site: Mild	34.8 (23.5 to 47.6)			
Pain at injection site: Moderate	47 (34.6 to 59.7)			
Pain at injection site: Severe	6.1 (1.7 to 14.8)			
Redness: Any	25.8 (15.8 to 38)			
Redness: Mild	6.1 (1.7 to 14.8)			
Redness: Moderate	18.2 (9.8 to 29.6)			
Redness: Severe	1.5 (0 to 8.2)			
Swelling: Any	19.7 (10.9 to 31.3)			
Swelling: Mild	13.6 (6.4 to 24.3)			
Swelling: Moderate	6.1 (1.7 to 14.8)			
Swelling: Severe	0 (0 to 5.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 1

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 1[4]

End point description:

Systemic events (fever [oral temperature >=38 degrees Celsius {C}], vomiting, diarrhea, headache, fatigue, chills, muscle pain other than muscle pain at the injection site, and joint pain), were reported using an electronic diary. Vaccination 1 safety population included all subjects who received at least 1 dose of Bexsero vaccine and had safety information available from Vaccination 1 until prior to Vaccination 2.

End point type	Primary

End point timeframe:

Within 7 days after Vaccination 1

Notes:

[4] - 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: Only descriptive data was planned to be reported for this endpoint.

End point values	Bexsero			
Subject group type	Reporting group			
Number of subjects analysed	68			
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C	1.5 (0 to 7.9)			
Fever 38 to <38.5 degrees C	1.5 (0 to 7.9)			
Fever 38.5 to <39 degrees C	0 (0 to 5.3)			
Fever 39 to 40 degrees C	0 (0 to 5.3)			
Fever >40 degrees C	0 (0 to 5.3)			
Vomiting: Any	1.5 (0 to 7.9)			
Vomiting: Mild	1.5 (0 to 7.9)			
Vomiting: Moderate	0 (0 to 5.3)			
Vomiting: Severe	0 (0 to 5.3)			
Diarrhea: Any	16.2 (8.4 to 27.1)			
Diarrhea: Mild	13.2 (6.2 to 23.6)			
Diarrhea: Moderate	2.9 (0.4 to 10.2)			
Diarrhea: Severe	0 (0 to 5.3)			
Headache: Any	45.6 (33.5 to 58.1)			
Headache: Mild	26.5 (16.5 to 38.6)			
Headache: Moderate	17.6 (9.5 to 28.8)			
Headache: Severe	1.5 (0 to 7.9)			
Fatigue: Any	55.9 (43.3 to 67.9)			
Fatigue: Mild	29.4 (19 to 41.7)			
Fatigue: Moderate	25 (15.3 to 37)			
Fatigue: Severe	1.5 (0 to 7.9)			
Chills: Any	26.5 (16.5 to 38.6)			
Chills: Mild	23.5 (14.1 to 35.4)			
Chills: Moderate	2.9 (0.4 to 10.2)			
Chills: Severe	0 (0 to 5.3)			
Muscle pain: Any	16.2 (8.4 to 27.1)			
Muscle pain: Mild	7.4 (2.4 to 16.3)			
Muscle pain: Moderate	7.4 (2.4 to 16.3)			
Muscle pain: Severe	1.5 (0 to 7.9)			
Joint pain: Any	17.6 (9.5 to 28.8)			

Joint pain: Mild	11.8 (5.2 to 21.9)			
Joint pain: Moderate	5.9 (1.6 to 14.4)			
Joint pain: Severe	0 (0 to 5.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 2

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 2[5]

End point description:

Systemic events (fever [oral temperature >=38 degrees C], vomiting, diarrhea, headache, fatigue, chills, muscle pain other than muscle pain at the injection site, and joint pain), were reported using an electronic diary. Vaccination 2 safety population included all subjects who received at least 1 dose of Bexsero vaccine and had safety information available from Vaccination 2 to post Vaccination 2 blood drawn.

End point type	Primary

End point timeframe:

Within 7 days after Vaccination 2

Notes:

[5] - 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: Only descriptive data was planned to be reported for this endpoint.

End point values	Bexsero			
Subject group type	Reporting group			
Number of subjects analysed	66			
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C	3 (0.4 to 10.5)			
Fever 38 to <38.5 degrees C	1.5 (0 to 8.2)			
Fever 38.5 to <39 degrees C	0 (0 to 5.4)			
Fever 39 to 40 degrees C	1.5 (0 to 8.2)			
Fever >40 degrees C	0 (0 to 5.4)			
Vomiting: Any	3 (0.4 to 10.5)			
Vomiting: Mild	3 (0.4 to 10.5)			
Vomiting: Moderate	0 (0 to 5.4)			
Vomiting: Severe	0 (0 to 5.4)			
Diarrhea: Any	4.5 (0.9 to 12.7)			
Diarrhea: Mild	4.5 (0.9 to 12.7)			
Diarrhea: Moderate	0 (0 to 5.4)			
Diarrhea: Severe	0 (0 to 5.4)			
Headache: Any	37.9 (26.2 to 50.7)			
Headache: Mild	21.2 (12.1 to 33)			

Headache: Moderate	16.7 (8.6 to 27.9)			
Headache: Severe	0 (0 to 5.4)			
Fatigue: Any	57.6 (44.8 to 69.7)			
Fatigue: Mild	33.3 (22.2 to 46)			
Fatigue: Moderate	18.2 (9.8 to 29.6)			
Fatigue: Severe	6.1 (1.7 to 14.8)			
Chills: Any	18.2 (9.8 to 29.6)			
Chills: Mild	16.7 (8.6 to 27.9)			
Chills: Moderate	0 (0 to 5.4)			
Chills: Severe	1.5 (0 to 8.2)			
Muscle pain: Any	16.7 (8.6 to 27.9)			
Muscle pain: Mild	9.1 (3.4 to 18.7)			
Muscle pain: Moderate	7.6 (2.5 to 16.8)			
Muscle pain: Severe	0 (0 to 5.4)			
Joint pain: Any	10.6 (4.4 to 20.6)			
Joint pain: Mild	3 (0.4 to 10.5)			
Joint pain: Moderate	7.6 (2.5 to 16.8)			
Joint pain: Severe	0 (0 to 5.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Use of Antipyretic Medication Within 7 Days After Vaccination 1

End point title	Percentage of Subjects With Use of Antipyretic Medication Within 7 Days After Vaccination 1[6]

End point description:

Vaccination 1 safety population included all subjects who received at least 1 dose of Bexsero vaccine and had safety information available from Vaccination 1 until prior to Vaccination 2.

End point type	Primary

End point timeframe:

Within 7 days after Vaccination 1

Notes:

[6] - 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: Only descriptive data was planned to be reported for this endpoint.

End point values	Bexsero			
Subject group type	Reporting group			
Number of subjects analysed	68			
Units: Percentage of subjects				
number (confidence interval 95%)				
Antipyretic medication use in presence of fever	0 (0 to 6.8)			
Antipyretic medication use in absence of fever	17.6 (8.3 to 31.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Use of Antipyretic Medication Within 7 Days After Vaccination 2

End point title	Percentage of Subjects With Use of Antipyretic Medication Within 7 Days After Vaccination 2[7]

End point description:

Vaccination 2 safety population included all subjects who received at least 1 dose of Bexsero vaccine and had safety information available from Vaccination 2 to post Vaccination 2 blood drawn.

End point type	Primary

End point timeframe:

Within 7 days after Vaccination 2

Notes:

[7] - 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: Only descriptive data was planned to be reported for this endpoint.

End point values	Bexsero			
Subject group type	Reporting group			
Number of subjects analysed	66			
Units: Percentage of subjects				
number (confidence interval 95%)				
Antipyretic medication use in presence of fever	3 (0.3 to 12.5)			
Antipyretic medication use in absence of fever	7.6 (2.1 to 19)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Vaccination 1 (Day 1) to 5 months after last administration of Bexsero

Adverse event reporting additional description:

Same event may appear as both an adverse event (AE) and serious AE (SAE). An event may be categorized as SAE in 1 subject and as nonserious in other subject, or 1 subject may have experienced both SAE and nonserious during the study. Safety population included all subjects who received at least 1 dose of Bexsero vaccine, had safety data available.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Bexsero

Reporting group description:

Subjects received at least 1 vaccination of Bexsero at Month 0,-2 visits.

Serious adverse events	Bexsero		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 68 (2.94%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Meningism			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Bexsero		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 68 (44.12%)		
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	4 / 68 (5.88%)		
occurrences (all)	4		
Clavicle fracture			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Concussion			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Hand fracture			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Road traffic accident			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Upper limb fracture			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 68 (4.41%)		
occurrences (all)	3		
Sensory loss			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain upper			

subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Diarrhea			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Chondropathy			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 68 (7.35%)		
occurrences (all)	6		
Otitis media			
subjects affected / exposed	4 / 68 (5.88%)		
occurrences (all)	4		
Pharyngitis			
subjects affected / exposed	4 / 68 (5.88%)		
occurrences (all)	7		
Gastrointestinal infection			
subjects affected / exposed	2 / 68 (2.94%)		
occurrences (all)	2		
Conjunctivitis			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Ear infection			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Gastroenteritis			

subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Infectious mononucleosis			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Skin infection			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Tinea pedis			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Wound infection			
subjects affected / exposed	1 / 68 (1.47%)		
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

None reported