



## Clinical trial results:

### Babies born Early Antibody Response to Men B vaccination: BEAR Men B

#### Summary

EudraCT number	2017-001487-38
Trial protocol	GB
Global end of trial date	28 August 2020

#### Results information

Result version number	v1 (current)
This version publication date	24 February 2023
First version publication date	24 February 2023
Summary attachment (see zip file)	Final report Bear Men B (Short report for MHRA_final.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	16.0247
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03125616
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	St George's University of London
Sponsor organisation address	Cranmer Terrace , London, United Kingdom,
Public contact	Paul Heath , St George's, University of London, pheath@sgul.ac.uk
Scientific contact	Paul Heath, St George's, University of London, pheath@sgul.ac.uk

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	26 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 August 2020
Global end of trial reached?	Yes
Global end of trial date	28 August 2020
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To compare the immune responses of infants born prematurely to Men B vaccination after two primary doses at 2 and 4 months of age compared with three primary doses at 2, 3 and 4 months of age.

Protection of trial subjects:

Anaesthetic instructions given to participants for the injection site to minimise distress.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 July 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	United Kingdom: 136
Worldwide total number of subjects	136
EEA total number of subjects	0

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)	136
Children (2-11 years)	0
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:

A total of 145 babies were recruited into the study

### Pre-assignment

Screening details:

Screening identified 392 potentially eligible participants, of whom 247 were excluded. A total of 145 babies were recruited into the study

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	Control
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Arm description: -

Arm type	Control
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Investigational medicinal product name	Bexsero
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Injection
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Routes of administration	Injection
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Dosage and administration details:

One dose (0.5 ml)

given at 2,4 and 12 months of age

<b>Arm title</b>	Trial arm
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Arm description: -

Arm type	Experimental
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Investigational medicinal product name	Bexsero
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Injection
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Routes of administration	Injection
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Dosage and administration details:

One dose (0.5 ml)

given at 2, 3, 4 and 12 months of age

<b>Number of subjects in period 1</b>	Control	Trial arm
Started	67	69
Completed	64	68
Not completed	3	1
Adverse event, serious fatal	2	-
Consent withdrawn by subject	1	1



## Baseline characteristics

## End points

### End points reporting groups

Reporting group title	Control
Reporting group description:	-
Reporting group title	Trial arm
Reporting group description:	-

### Primary: hSBA GMTs one month after completing primary immunisations for relevant 4CMenB antigens: fHbp

End point title	hSBA GMTs one month after completing primary immunisations for relevant 4CMenB antigens: fHbp
End point description:	
End point type	Primary
End point timeframe:	1 month

End point values	Control	Trial arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	68		
Units: Geometric Mean Titre (GMT)				
geometric mean (confidence interval 95%)	40.5 (31.2 to 52.6)	27.7 (20.4 to 37.7)		

<b>Attachments (see zip file)</b>	All results/Bear study_AC.xlsx
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### Statistical analyses

<b>Statistical analysis title</b>	fHbp
Comparison groups	Control v Trial arm
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13
Method	Kruskal-wallis

### Primary: hSBA GMTs one month after completing primary immunisations for relevant 4CMenB antigens: NadA

End point title	hSBA GMTs one month after completing primary immunisations for relevant 4CMenB antigens: NadA
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End point description:

End point type Primary

End point timeframe:  
1 month

<b>End point values</b>	Control	Trial arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	68		
Units: Geometric Mean Titre (GMT)				
geometric mean (confidence interval 95%)	481.1 (387.6 to 597.6)	603.7 (509.8 to 715.5)		

### Statistical analyses

<b>Statistical analysis title</b>	NadA
Comparison groups	Trial arm v Control
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.19
Method	Kruskal-wallis

### Primary: hSBA GMTs one month after completing primary immunisations for relevant 4CMenB antigens: PorA

End point title hSBA GMTs one month after completing primary immunisations for relevant 4CMenB antigens: PorA

End point description:

End point type Primary

End point timeframe:  
1 month

<b>End point values</b>	Control	Trial arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	68		
Units: Geometric Mean Titre (GMT)				
geometric mean (confidence interval 95%)	8.7 (5.9 to 12.9)	11.1 (8.4 to 14.8)		

## Statistical analyses

<b>Statistical analysis title</b>	PorA
Comparison groups	Control v Trial arm
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4
Method	Kruskal-wallis

## Primary: hSBA proportions $\geq$ 1:4, one month after completing primary immunisations for relevant 4CMenB antigens: fHbp

End point title	hSBA proportions $\geq$ 1:4, one month after completing primary immunisations for relevant 4CMenB antigens: fHbp
End point description:	
End point type	Primary
End point timeframe:	1 month

<b>End point values</b>	Control	Trial arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	68		
Units: Percentage				
geometric mean (confidence interval 95%)	98 (90 to 100)	94 (85 to 98)		

## Statistical analyses

<b>Statistical analysis title</b>	fHbp
Comparison groups	Control v Trial arm
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.37
Method	Fisher exact

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**Secondary: hSBA proportions  $\geq$  1:4, one month after completing primary immunisations for relevant 4CMenB antigens: NadA**

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End point title	hSBA proportions $\geq$ 1:4, one month after completing primary immunisations for relevant 4CMenB antigens: NadA
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End point description:

End point type	Secondary
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End point timeframe:

1 month

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<b>End point values</b>	Control	Trial arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	68		
Units: percentage				
geometric mean (confidence interval 95%)	100 (94 to 100)	100 (94 to 100)		

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: hSBA proportions  $\geq$  1:4, one month after completing primary immunisations for relevant 4CMenB antigens: PorA**

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End point title	hSBA proportions $\geq$ 1:4, one month after completing primary immunisations for relevant 4CMenB antigens: PorA
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End point description:

End point type	Secondary
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End point timeframe:

1 month

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<b>End point values</b>	Control	Trial arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	68		
Units: Percentage				
geometric mean (confidence interval 95%)	70 (70 to 70)	87 (87 to 87)		

## Statistical analyses

<b>Statistical analysis title</b>	PorA
Comparison groups	Control v Trial arm
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	Fisher exact

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

28 days

Assessment type	Systematic
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### Dictionary used

Dictionary name	DAIDS
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Dictionary version	2.1
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### Reporting groups

Reporting group title	Control
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Reporting group description: -

Reporting group title	Trial arm
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Reporting group description: -

<b>Serious adverse events</b>	Control	Trial arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	49 / 67 (73.13%)	51 / 69 (73.91%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events	1	0	
Cardiac disorders			
Hypertension			
subjects affected / exposed	1 / 67 (1.49%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patent Ductus Arteriosus ligation			
subjects affected / exposed	0 / 67 (0.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 67 (0.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Collapse			

subjects affected / exposed	1 / 67 (1.49%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
post haemorrhagic hydrocephalus			
subjects affected / exposed	1 / 67 (1.49%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infantile spasms			
subjects affected / exposed	0 / 67 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleepy			
subjects affected / exposed	0 / 67 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Elective admission for vaccination following previous instability			
subjects affected / exposed	1 / 67 (1.49%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinopathy of Prematurity			

subjects affected / exposed	1 / 67 (1.49%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Gastrointestinal disorders</b>			
<b>Inguinal hernia</b>			
subjects affected / exposed	2 / 67 (2.99%)	3 / 69 (4.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Vomiting</b>			
subjects affected / exposed	2 / 67 (2.99%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Choking</b>			
subjects affected / exposed	1 / 67 (1.49%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Constipation</b>			
subjects affected / exposed	1 / 67 (1.49%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Gastro-oesophageal reflux disease</b>			
subjects affected / exposed	0 / 67 (0.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Gastroenteritis</b>			
subjects affected / exposed	0 / 67 (0.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Diarrhoea</b>			
subjects affected / exposed	0 / 67 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Poor feeding infant</b>			

subjects affected / exposed	0 / 67 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileostomy			
subjects affected / exposed	0 / 67 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchiolitis			
subjects affected / exposed	14 / 67 (20.90%)	5 / 69 (7.25%)	
occurrences causally related to treatment / all	0 / 14	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 1	
Respiratory distress			
subjects affected / exposed	5 / 67 (7.46%)	6 / 69 (8.70%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	2 / 67 (2.99%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Refractory respiratory failure			
subjects affected / exposed	1 / 67 (1.49%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Apnoea			
subjects affected / exposed	4 / 67 (5.97%)	3 / 69 (4.35%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Increased work of breathing			
subjects affected / exposed	1 / 67 (1.49%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stridor			

subjects affected / exposed	1 / 67 (1.49%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Cough</b>			
subjects affected / exposed	0 / 67 (0.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Tracheostomy formation</b>			
subjects affected / exposed	0 / 67 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Increased oxygen requirements</b>			
subjects affected / exposed	0 / 67 (0.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Skin and subcutaneous tissue disorders</b>			
<b>Rash</b>			
subjects affected / exposed	0 / 67 (0.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Musculoskeletal and connective tissue disorders</b>			
<b>Neuromuscular weakness</b>			
subjects affected / exposed	0 / 67 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Infections and infestations</b>			
<b>coryzal</b>			
subjects affected / exposed	1 / 67 (1.49%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Urinary tract infection</b>			
subjects affected / exposed	2 / 67 (2.99%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Viral infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaccination reaction causing fever			
subjects affected / exposed	1 / 67 (1.49%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin swelling			
subjects affected / exposed	0 / 67 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
cow milk intolerancia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	Control	Trial arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 67 (1.49%)	9 / 69 (13.04%)	
Infections and infestations			
Fever			
subjects affected / exposed	1 / 67 (1.49%)	9 / 69 (13.04%)	
occurrences (all)	1	9	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 August 2019	<p>Respective SmPC for NIMPs updates: Prevenar 13 suspension for injection updated 01-May-2019; Rotarix Oral Applicator updated 03-Apr-2019; Priorix updated 24-Jan-2019; Menitorix updated 08-Mar-2016</p> <p>Respective SmPC for NIMPs addition of Infanrix hexa, Powder and suspension for suspension for injection 15-Feb-2019 to substitute INFANRIX-IPV+Hib 25-Apr-2017</p> <p>Protocol changes: primarily the study completion date for March 2020 BearMenB Protocol version 2.1, 2nd Aug 2018 TC BearMenB Protocol version 2.1, 2nd Aug 2018</p> <p>Sponsor Contact Details: Change Debbie Rolfe [Regulatory Assurance Manager] to Subhir Bedi [Head of Research Governance and Delivery]</p> <p>We would like to inform the removal of the non-IMP Pediacel syringe 19th Feb 2017 from the study.</p>

Notes:

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### 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.

N/A

Notes: