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

Background

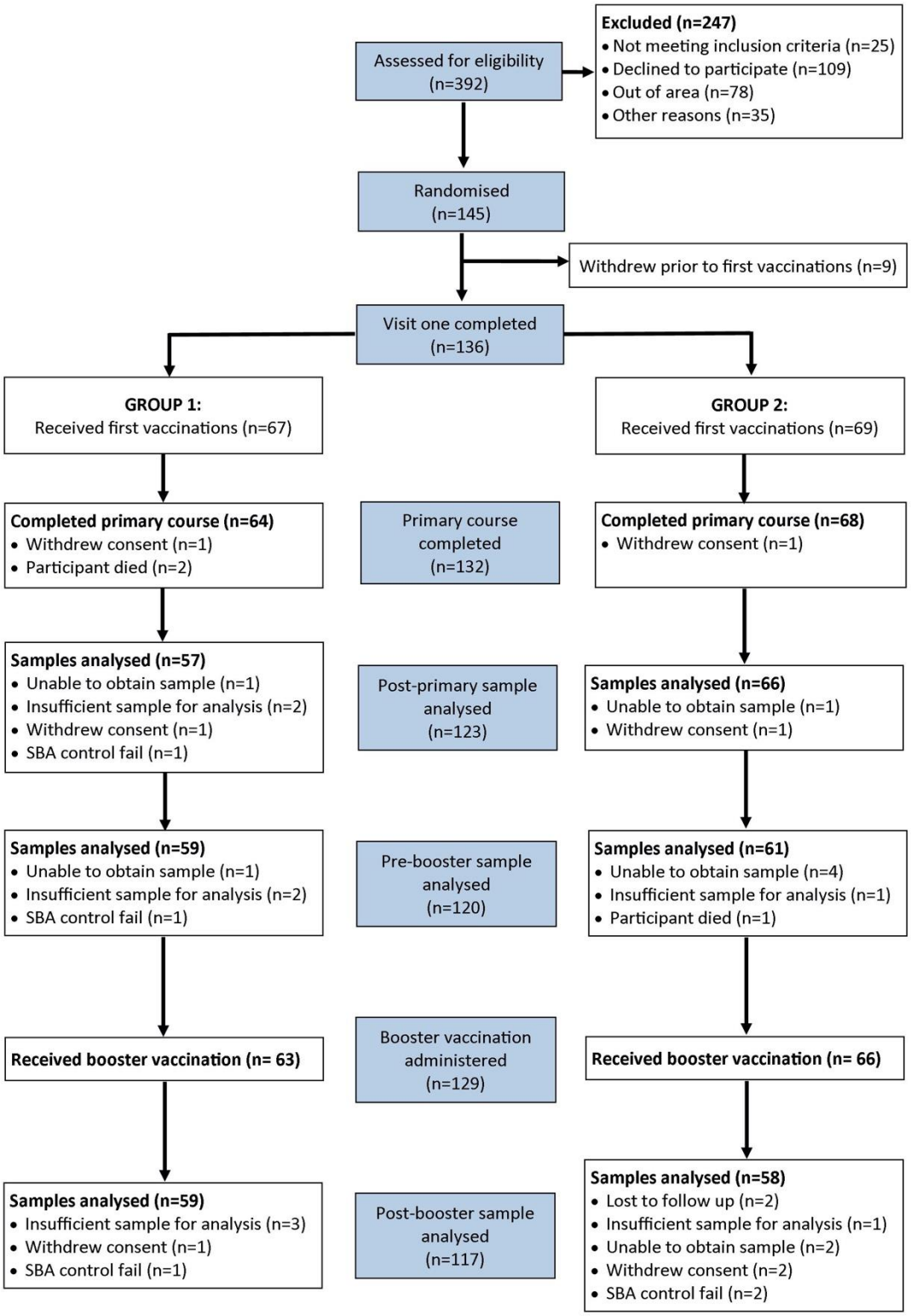
Bexsero was licensed in 2013 by the European Medicines Agency to be given according to a three-dose priming schedule followed by a booster in the second year of life. After extensive discussion about cost effectiveness, Bexsero was introduced in the UK according to a reduced 2+1 schedule in 2015, with doses being given at 2, 4 and 12 months. There are currently no immunogenicity studies of this schedule in preterm infants.

The BEAR Men B study was a multicentre study across six UK sites in which preterm babies born at <35 weeks (50% born at <30 weeks) were randomised to one of two Bexsero schedules: 2+1 (2, 4 and 12 months) or 3+1 (2, 3, 4 and 12 months).

Results

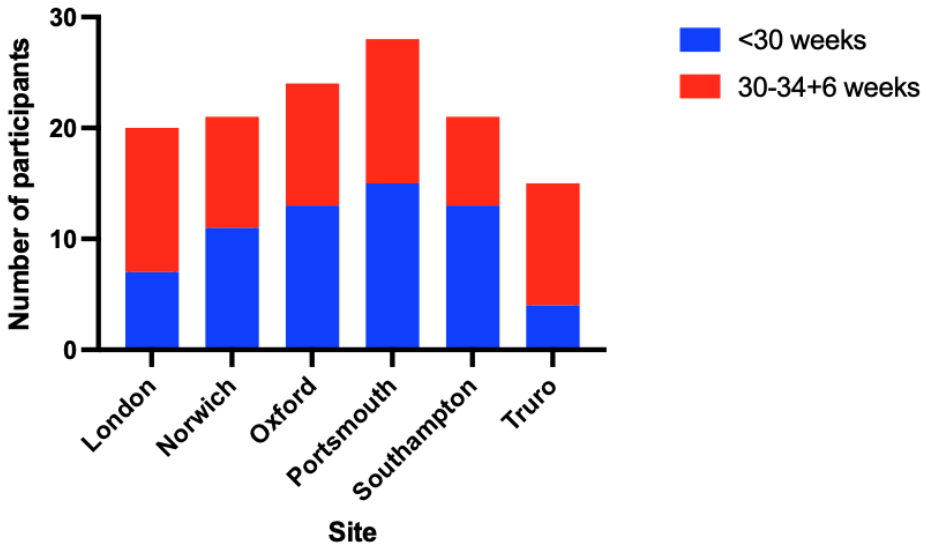
Screening identified 392 potentially eligible participants, of whom 247 were excluded. A total of 145 babies were recruited into the study; 9 babies withdrew before receiving their first vaccinations and were therefore not included in the total number of recruits. 136 babies completed the first study visit and are considered to be participants in the study. 124 infants completed the study; three babies died, seven were withdrawn and two lost to follow up. For seven of the withdrawn babies there was no confirmation of consent from the parents that their data could be used; these were removed from the analysis. There are therefore 129 babies included in the analysis. The progress of participants in the study is shown in the CONSORT flow diagram (Figure 1).

Figure 1: CONSORT flow diagram for BEAR Men B



We recruited from six UK sites. The distribution of recruits by gestational age varied by site (figure 2).

Figure 2: Recruitment by gestational age category and site



Demographics

The baseline characteristics of study participants are shown in table 1. Chronic lung disease was defined as supplementary oxygen +/- mechanical ventilation at >28 days of life and at a corrected gestational age of >36 gestational weeks. Small for gestational age (SGA) was defined as <10th percentile for gestational age.

Table 1: Baseline characteristics

Characteristic	N	Group 1 (2+1 schedule)	N	Group 2 (3+1 schedule)
Gestational age Median (range)	64	30^{+2} (23^{+0}-34^{+3})	65	30^{+2} (24^{+2}-34^{+3})
Ethnicity (white) Number (%)	64	52 (81.3)	65	57 (87.7)
Sex (female) Number (%)	64	32 (50)	65	41 (63.1)
Birthweight (g) Median (range)	64	1262.5 (575-2790)	65	1350 (490-2610)
CLD Number (%)	64	17 (26.6)	65	15 (23.1)
SGA	64		65	

Number (%)		5 (7.8)		10 (15.4)
Blood transfusion Number (%)	64	25 (39.1)	65	27 (41.5)
Antenatal steroids Number (%)	64	59 (92.2)	65	63 (96.9)
Postnatal steroids Number (%)	64	5 (7.8)	65	2 (3.1)

CLD Chronic Lung Disease; SGA Small for Gestational Age; g grams

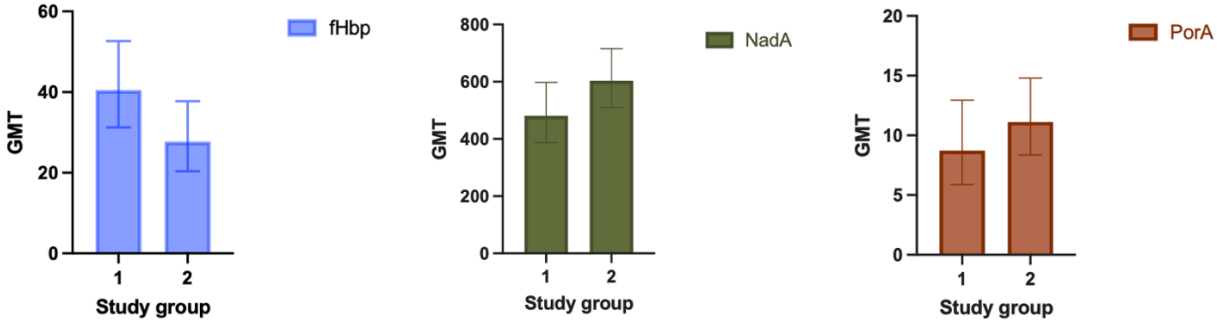
Immunogenicity

Babies had blood sampling performed at 5 months (1 month after completing primary vaccinations), 12 months (pre-booster) and 13 months (post booster). Results were compared between study groups.

Five months

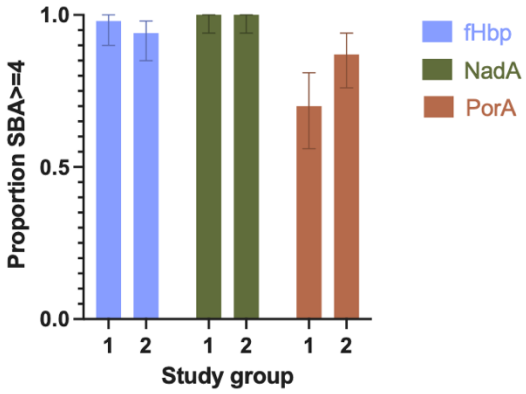
The results at five months of age are shown in figure 3.

Figure 3: GMT (95% CI) at five months for SBA titres for fHbp, NadA and PorA according to study group



There were no statistically significant differences between groups when analysed together, but for babies born at 30-34+6 weeks there was a borderline difference for PorA (p=0.048) and a significant difference for NadA (p=0.02), with those who received a 3+1 schedule having higher titres. The proportion of babies achieving a titre of ≥1:4 was significantly higher for babies who received the 3+1 schedule for Por A (p=0.03) while no differences between groups was seen for the other two tested antigens (figure 4).

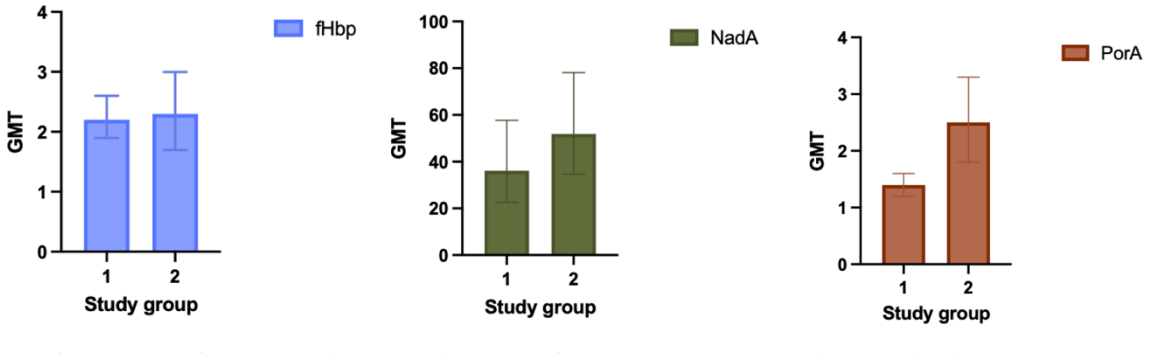
Figure 4: Proportions of infants achieving GMTs ≥1:4 at five months for each tested antigen according to study group



Twelve months

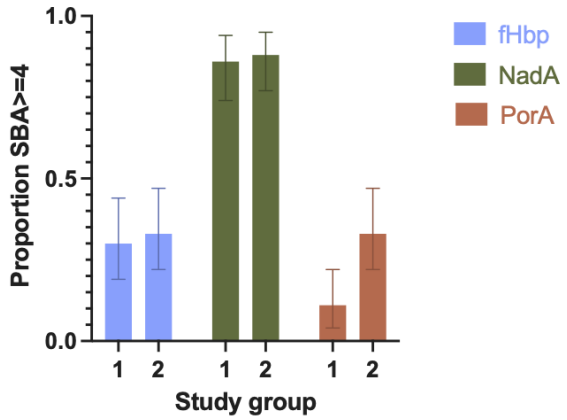
The results at twelve months of age are shown in figure 5.

Figure 5: GMT (95% CI) at twelve months for SBA titres for fHbp, NadA and PorA according to study group



There was a significant difference between study groups for PorA (p=0.002) with those who received a 3+1 schedule having higher titres. When the groups were analysed separately, this difference was not seen in babies born at less than 30 weeks, but was seen in those born at a later gestation (p=0.003). The proportion of babies achieving a titre of ≥1:4 for PorA was again significantly higher for babies who received the 3+1 schedule (p=0.004) while no differences between groups was seen for the other two tested antigens (figure 6).

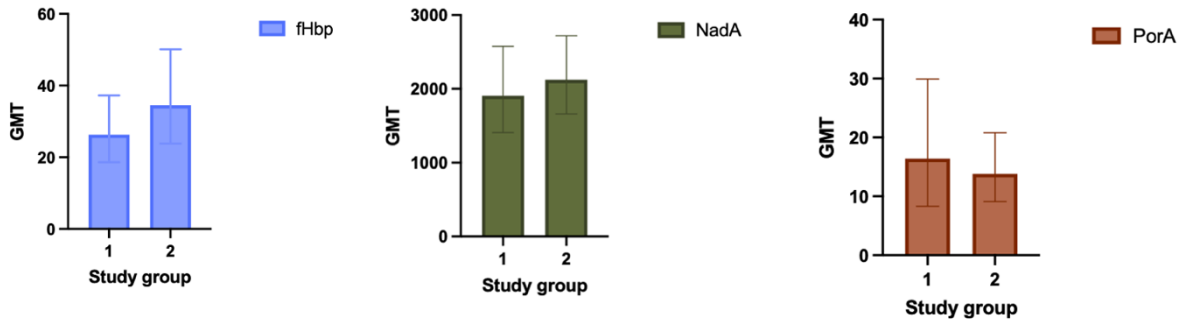
Figure 6: Proportions of infants achieving GMTs ≥1:4 at twelve months for each tested antigen according to study group



Thirteen months

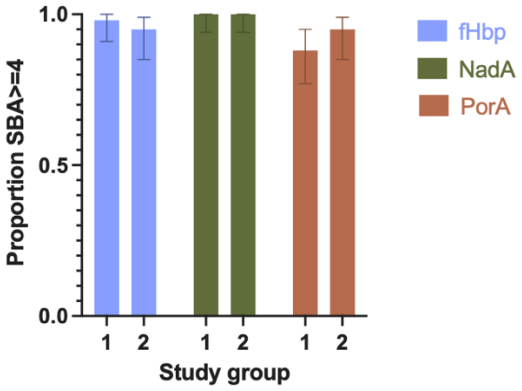
The results at thirteen months of age are shown in figure 7.

Figure 7: GMT (95% CI) at thirteen months for SBA titres for fHbp, NadA and PorA according to study group



There were no differences between study groups when analysed together. When the results were analysed separately, there was a significant difference in fHbp for those babies born at less than 30 weeks, with higher titres in the group who received a 3+1 schedule. There were no differences observed in babies born at 30-34+6 weeks. There were no differences in proportions of babies achieving titres of ≥1:4 (figure 8).

Figure 8: Proportions of infants achieving GMTs ≥1:4 at thirteen months for each tested antigen according to study group



Overall protection

When we used a composite cut off for protection of ≥1:4 for ≥2/3 of the tested antigens we found no significant differences between groups at any of the time points when the population was analysed together or separately according to gestational age.

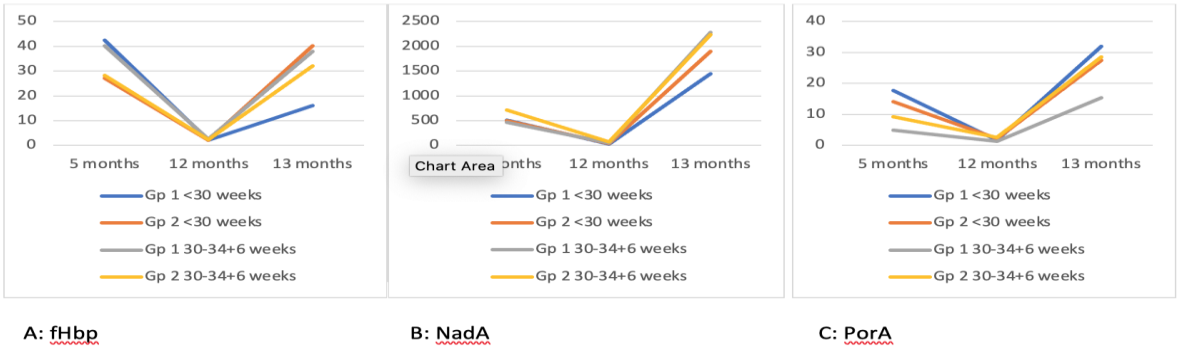
Fold changes

Fold changes post-primary to post-booster and pre-booster to post-booster are shown in table 2. The response to booster vaccination against fHbp in group one was less than that seen to primary vaccination and the response in group 2 was not elevated (table 2).

Table 2: Fold changes post-primary to booster and pre-booster to post-booster

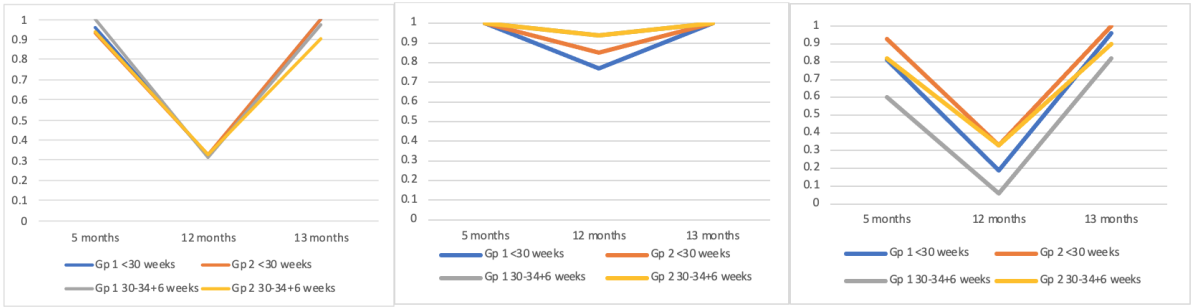
	fHbp		NadA		PorA	
	Group 1	**Group 2**	**Group 1**	**Group 2**	**Group 1**	**Group 2**
Fold change post primary to post booster	0.7 (0.5-1.0)	1.2 (0.8-1.8)	3.9 (2.8-5.3)	3.2 (2.5-4.1)	2.6 (1.7-3.9)	2.3 (1.6-3.4)
Fold change pre-booster to post-booster	14.0 (10.4-18.9)	15.2 (10.9-21.2)	52.6 (36.8-75.1)	41.5 (28.7-59.9)	17.5 (11.8-26.0)	11.0 (7.2-16.6)

Figure 9: GMTs at 5, 12 and 13 months according to group and gestational age



A: fHbp B: NadA C: PorA

Figure 10: Proportions ≥1:4 at 5, 12 and 13 months according to group and gestational age



Reactogenicity

Adverse Events (AEs), Serious Adverse Events (SAEs) and Suspected Unexpected Serious Adverse Reactions (SUSARs)

There were three SUSARs reported during the trial involving two participants, one from each study group. One SUSAR consisted of increasing desaturations, bradycardias and apnoeas on the day following vaccination and the other two were episodes of apnoea after vaccination at two and four months of age. Although the SmPC includes apnoea as a possible adverse event following vaccination, this is only referred to in the context of infants born at less than 28 weeks of gestation. Both episodes of apnoea were in the same participant, born at 32+5 weeks and these were therefore considered to be unexpected and recorded as a SUSAR. The other participant, born at a gestation of 26+1 weeks, experienced desaturations, bradycardia and apnoea soon after vaccination.

Three babies died during the study (two from group one, one from group two) and none of these deaths were considered to be related to vaccination. The first baby was born at 29+2 weeks of gestation and was admitted to hospital nine days after receiving his first vaccinations with apnoeic episodes and was later diagnosed with RSV bronchiolitis; the second baby was born at 24+5 weeks of gestation and was admitted to hospital four months after completing her primary vaccinations with increased work of breathing and was

later diagnosed with rhinovirus bronchiolitis; the third baby was born at 25+3 weeks of gestation and experienced a sudden, unexpected (and unexplained) collapse in hospital six weeks after receiving her first vaccinations.

There were 101 SAEs reported as part of the study, one of these was reported in a baby who was withdrawn from the study prior to receiving their first vaccinations and has therefore not been included. The large number of reported SAEs reflect the fragility of this preterm population and, of note, the majority of the SAEs (n=73) occurred in those babies born at less than 30 weeks of gestation. A summary of the recorded SAEs is shown in table 3.

Table 3: Table of recorded SAEs according to group

Group 1	**N= 49**	**Group 2**	**N=51**
Inguinal hernia	2	Infantile spasms	1
Coryzal, febrile and poor feeding	1	Inguinal hernia repair	3
Bronchiolitis	14	GORD	2
Respiratory distress	5	Apnoea	3
RTI	2	Respiratory distress	6
Cow's milk protein intolerance	1	Groin swelling	1
Anaemia	1	Cough	2
Vomiting and static growth	1	Gastroenteritis	2
UTI	2	Respiratory tract infection	1
Croup and bronchiolitis	1	PDA ligation	2
Refractory respiratory failure requiring ECMO	1	Bronchiolitis	5
Chronic lung disease and pulmonary hypertension	1	Tracheostomy formation	1
Increased work of breathing	2	Diarrhoea	1
Choking episode	1	Respiratory failure	1
Viral infection	1	Progression of ROP	1
Vomiting	1	Increased oxygen requirements	2
Sudden unexpected collapse	1	Constipation	1
Elective admission for vaccination following previous instability	1	Elective admission for vaccination following previous instability	1
Apnoea	4	Stridor	1
Increased work of breathing and groin swelling	1	Rash	1
		Increased work of breathing	2
Stridor	1	Sleepy	1
Progression of ROP	1	Right groin swelling and distress	1
Constipation	1	Non-blanching rash	1

Worsening post haemorrhagic hydrocephalus	1	Poor feeding	1
Vaccination reaction causing fever	1	Cardiac failure	2
		Hypertension	1
		Neuromuscular weakness	1
		Altered mental state secondary to hyponatraemia	1
		Intestinal prolapse through ileostomy	1
		Fever	1

GORD Gastro-oesophageal reflux disease; RTI Respiratory Tract Infection; UTI Urinary Tract Infection; PDA Patent Ductus Arteriosus; ECMO Extracorporeal Membrane Oxygenation; ROP Retinopathy of Prematurity

Parents/carers were asked to complete a diary for seven days following each vaccination in which information was collected about local and systemic reactions, fever and medical attendance.

Cardiorespiratory instability

Those participants who were vaccinated in hospital had additional information collected about their cardiorespiratory status for the period of 24 hours before and 72 hours after vaccination.

84 vaccination episodes took place in hospital, involving 56 participants (Table 4). Babies vaccinated in hospital had significantly lower gestational age and birthweights and a significantly higher rate of CLD at all three monitored visits. At V3 the age at study visit was also significantly different between groups (table 5).

Table 4: Participants vaccinated in hospital according to group

	Group 1		**Group 2**	
	<30 weeks	**30-34+6 weeks**	**<30 weeks**	**30-34+6 weeks**
Visit 1 (n=56)	29	2	25	0
Visit 2 (n=20)	10	1	9	0
Visit 3 (n=8)	4	1	3	0

Table 5: Characteristics of those vaccinated in hospital compared with those not vaccinated in the NNU

	Not vaccinated in NNU	**Vaccinated in NNU**	**P**
V1			
Gestation (weeks)	32^{+2} (28^{+0}-34^{+3})	27^{+2} (23^{+0}-32^{+3})	**<0.005**

Birthweight (g)	1700 (930-2790)	925 (490-1605)	**<0.005**
SGA	10 (13.7)	5 (8.9)	0.58
CLD	3 (4.1%)	29 (51.8)	**<0.005**
Sex (female)	42 (57.5)	31 (55.4)	0.86
Age at V1 (days)	61 (51-94)	60.5 (52-84)	0.64
V2			
Gestation (weeks)	31^{+2} (25^{+3}-34^{+3})	25^{+5} (23^{+0}-30^{+6})	**<0.005**
Birthweight (g)	1449.5 (672-2610)	754 (490-1170)	**<0.005**
SGA	12 (11.1)	3 (15)	0.70
CLD	17 (15.7)	14 (70)	**<0.005**
Sex (female)	63 (58.3)	10 (50)	0.62
Age at V2 (days)	93 (80-131)	94 (82-138)	0.11
V3			
Gestation (weeks)	30^{+4} (24^{+2}-34^{+3})	25^{+5} (23-30^{+6})	**<0.005**
Birthweight (g)	1372 (580-2610)	669 (490-780)	**<0.005**
SGA	12 (10)	3 (37.5)	0.05
CLD	26 (21.7)	5 (62.5)	**0.02**
Sex (female)	70 (58.3)	3 (37.5)	0.29
Age at V3 (days)	124 (110-164)	136 (110-175)	**0.01**

A summary of cardiorespiratory status is recorded for visits 1-3 in table 6 and a summary for all vaccination episodes in table 7. Overall, apnoea, bradycardia and desaturation were recorded more frequently in the period following vaccination compared with the period prior to vaccination (table 7). At visit two, when those in study group 2 received an additional dose of Bexsero, there were no differences between vaccine schedules for ventilatory support (p= 0.15), episodes of apnoea (p=0.57), episodes of bradycardia (p=0.57), episodes of desaturation (p=0.62) or overall desaturation (p=0.64).

Table 6: Summary of cardiorespiratory status after vaccination (V1-V3)

Visit 1 (n=55)	**Deterioration**		**Stable**		**Improvem**	
Apnoea N (%)	10 (18.2)		43 (78.2)		2 (3.6)	
Bradycardia N (%)	12 (22.2)		38 (70.4)		4 (7.4)	
Desaturation N (%)	17 (31.5)		33 (61.1)		4 (7.4)	
Ventilatory support N (%)	12 (21.8)		42 (76.4)		1 (1.8)	
Overall N (%)	23 (42.6)		27 (50)		4 (7.4)	
Visit 2 (n=20)	**Gp 1 (n=11)**	**Gp 2 (n=9)**	**Gp 1 (n=11)**	**Gp 2 (n=9)**	**Gp 1 (n=11)**	**Gp**
Apnoea N (%)	1	2	10	6	0	1
Bradycardia N (%)	1	2	10	7	0	0
Desaturation N (%)	2	3	8	5	1	1
Ventilatory support N (%)	2	5	7	3	0	0
Overall N (%)	3	4	8	5	0	0
Visit 3 (n=8)						

Apnoea N (%)	0 (0)	7 (100)	0 (0)
Bradycardia N (%)	0 (0)	7 (100)	0 (0)
Desaturation N (%)	1 (14.3)	6 (85.7)	0 (0)
Ventilatory support	1 (20)	4 (80)	0 (0)
Overall N (%)	2 (28.6)	5 (71.4)	0 (0)

Table 7: Episodes of apnoea, bradycardia and desaturation for all vaccination episodes

	Any episode of apnoea reported	Any episode of bradycardia reported	Any episode of desaturation reported
Before Vaccination (n=84) **N (%)**	5 (6.0)	13 (15.5)	19 (22.6)
After Vaccination (n=82) **N (%)**	14 (17.1)	20 (24.4)	31 (37.8)

Fever

Fever within 7 days

Fever was a fairly common event, particularly following the 12-month vaccinations at which point 26% of participants had a fever and 7% a severe fever. At the time of the second immunisations, when those in study group 2 received an additional dose of Bexsero, there were significantly more episodes of fever reported in group 2 than group 1 (p=0.02) (table 8).

Table 8: Proportions of participants experiencing fever within 7 days following each vaccination visit

Visit	**Group**	**N**	**Any**		**Severe (>=grade 3)**		**P value**	
			n	**%**	**n**	**%**	**Any**	**Severe**
1	Combined	122	7	0.06 (0.03-0.12)	1	0.01 (0.001-0.06)		
2	Group 1	58	1	0.02 (-0.02-0.05)	0	0	0.02	1.0
	Group 2	64	9	0.14 (0.06-0.23)	1	0.02 (-0.01-0.05)		
3	Combined	112	19	0.17 (0.11-0.25)	0	0		
5	Combined	102	27	0.26 (0.19-0.36)	7	0.07 (0.03-0.14)		

Fever within 28 days

Fever after seven days, but within 28 days, was uncommon. It was highest after the booster vaccinations at 12 months, affecting 7.3% of participants. At visit 2, when study group 2 received an additional dose of Bexsero, no participants in either of the study groups had any fever reported within this period (table 9).

Table 9: Fever after 7 days, but within 28 days with comparison at V2

		N	Fever within 28 days n (%)	P value
Visit 1		129	2 (1.6)	
Visit 2	Gp. 1	63	0 (0)	0.50
	Gp. 2	65	0 (0)	
Visit 3		128	3 (2.3)	
Visit 5		124	9 (7.3)	

Systemic reactions

Systemic reactions following each of the vaccination visits are shown in table 10. There were no significant differences when study groups were compared at V2.

Table 10: Systemic reactions following each vaccination visit and divided according to group at visit 2

Visit	N	Adverse event	Group	Any		Severe		P value	
				n	Proportion (95% CI)	n	Proportion (95% CI)	Any	Severe
1	107	Reduced feeding	Combined	56	0.52 (0.43-0.62)	4	0.04 (0.01-0.10)		
	108	Reduced activity		71	0.66 (0.56-0.74)	21	0.20 (0.13-0.28)		
	103	Irritability		64	0.62 (0.52-0.71)	4	0.04 (0.01-0.10)		
	104	Crying		48	0.46 (0.37-0.56)	3	0.03 (0.01-0.09)		
	102	Vomiting		45	0.44 (0.35-0.54)	0	0		
	103	Diarrhoea		36	0.35 (0.26-0.45)	1	0.01 (0.001-0.07)		
2	106	Reduced feeding	Gp. 1 (n=51)	19	0.37 (0.24-0.51)	1	0.02 (-0.02-0.06)	0.12	0.48
			Gp. 2 (n=55)	29	0.53 (0.40-0.66)	0	0		
	107	Reduced activity	Gp. 1 (n=52)	24	0.46 (0.33-0.60)	1	0.02 (-0.02-0.06)	0.053	0.11
			Gp. 2 (n=55)	36	0.65 (0.53-0.78)	6	0.11 (0.03-0.19)		
	106	Irritability	Gp. 1 (n=51)	35	0.69 (0.56-0.81)	1	0.02 (-0.02-0.06)	1.0	0.37
			Gp. 2 (n=55)	38	0.69 (0.57-0.81)	4	0.07 (0.004-0.14)		
	106	Crying	Gp. 1 (n=51)	30	0.59 (0.45-0.72)	2	0.04 (-0.01-0.09)	0.56	1.0
			Gp. 2 (n=55)	29	0.53 (0.40-0.66)	3	0.05 (-0.005-0.11)		
	104	Vomiting	Gp 1 (n=50)	19	0.38 (0.25-0.51)	0	0	1.0	-

			Gp. 2 (n=54)	21	0.39 (0.26-0.52)	0	0		
	103	Diarrhoea	Gp 1 (n=50)	20	0.40 (0.26-0.54)	2	0.04 (-0.01-0.09)	0.052	0.23
			Gp 2 (n=53)	11	0.21 (0.10-0.32)	0	0		
3	101	Reduced feeding	Combined	50	0.50 (0.40-0.59)	3	0.03 (0.01-0.09)	[redacted]	
	102	Reduced activity		65	0.64 (0.54-0.73)	6	0.06 (0.03-0.13)		
	102	Irritability		84	0.82 (0.74-0.89)	11	0.11 (0.06-0.19)		
	102	Crying		68	0.67 (0.57-0.75)	3	0.03 (0.01-0.09)		
	100	Vomiting		40	0.4 (0.31-0.50)	2	0.02 (0.005-0.08)		
	101	Diarrhoea		27	0.27 (0.19-0.36)	2	0.02 (0.005-0.08)		
5	96	Reduced feeding	Combined	50	0.52 (0.42-0.62)	1	0.01 (0.001-0.07)		
	94	Reduced activity		50	0.53 (0.43-0.63)	5	0.05 (0.02-0.12)		
	96	Irritability		75	0.78 (0.69-0.85)	13	0.14 (0.08-0.22)		
	96	Crying		55	0.57 (0.47-0.67)	9	0.09 (0.05-0.17)		
	96	Vomiting		31	0.32 (0.24-0.42)	1	0.01 (0.001-0.07)		
	97	Diarrhoea		29	0.30 (0.22-0.40)	2	0.02 (0.01-0.08)		

Investigation for sepsis

The combination of fever and systemic symptoms can raise the suspicion of systemic illness or sepsis and investigation for sepsis after vaccination is widely described. The results for those investigated for sepsis and commenced on antibiotics within 7 and 28 days are shown in table 11. At visit two, when those in study group 2 received an additional dose of Bexsero, the rates in the study groups were compared and no difference was observed. The highest rates of investigation and treatment for sepsis were following V1 (4.7 % for both groups).

Table 11: Investigated for sepsis and started on antibiotics within 7 and 28 days

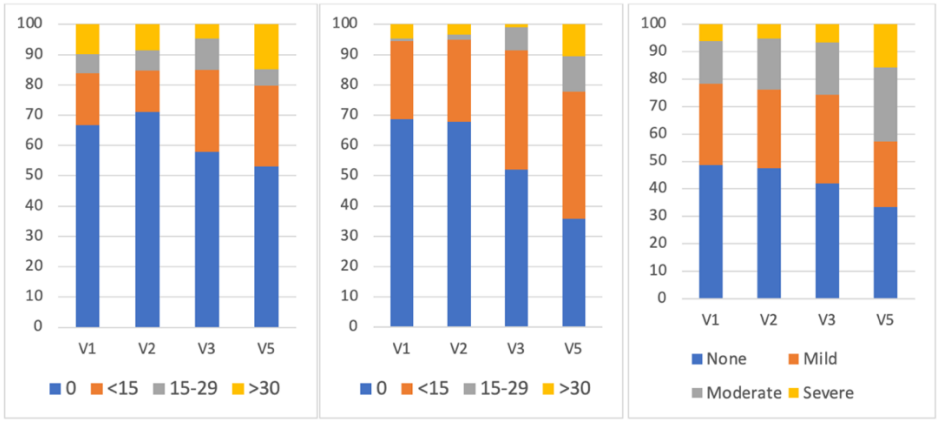
		N	**Investigated for sepsis and commenced on antibiotics within 7 days n (%)**	**P value**	**Investigated for sepsis and commenced on antibiotics within 28 days n (%)**	**P value**
Visit 1		129	6 (4.7)	-	6 (4.7)	
Visit 2	Gp. 1	63	2 (3.2)	1.0	1 (1.6)	0.50
	Gp. 2	65	2 (3.1)		0 (0)	
Visit 3		128	0 (0)	**-**	1 (0.78)	

Visit 5	126	0 (0)	-	0 (0)	

Local reactions

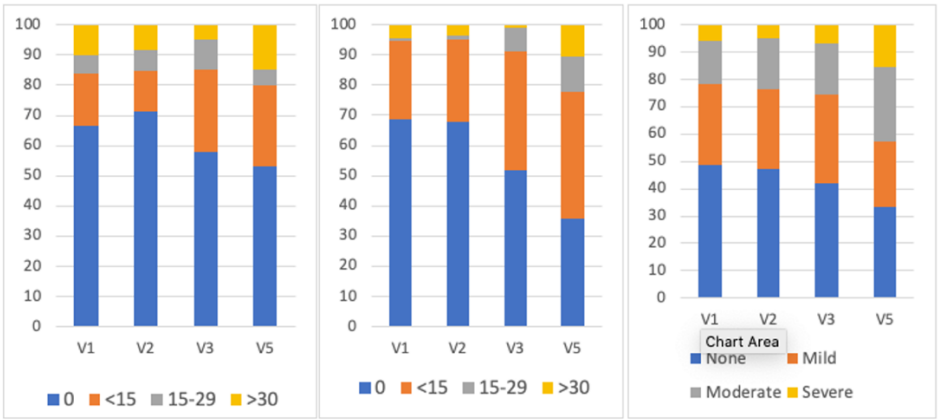
Local reactions were common after all study vaccinations and are shown according to vaccine in figures 11-15 and overall, by vaccine doses administered, in figure 16. Pain was the most commonly reported local side effect, and this was particularly frequent following vaccination with Bexsero.

Figure 11: Graphs of local reactions experienced following Bexsero vaccination



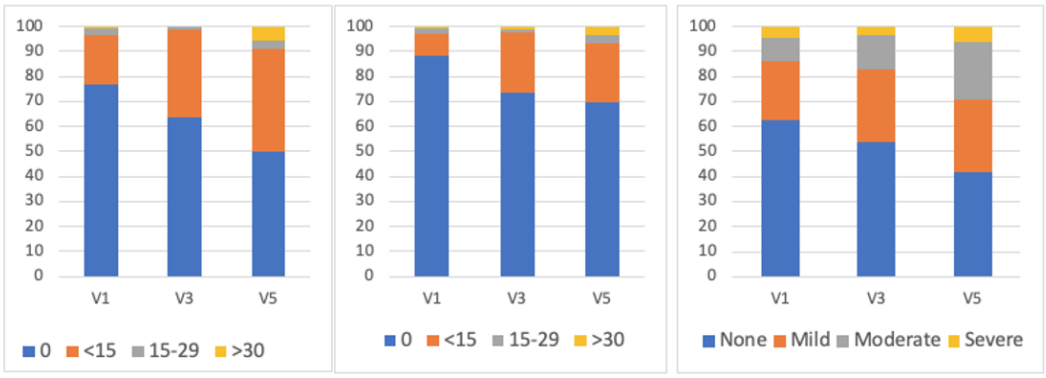
A: Erythema B: Swelling C: Tenderness

Figure 12: Graphs of local reactions experienced following Prevenar vaccination



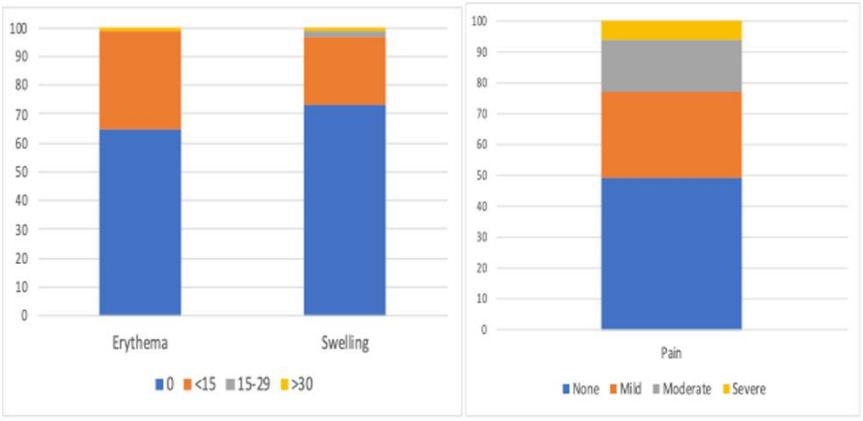
A: Erythema B: Swelling C: Tenderness

Figure 13: Graphs of local reactions experienced following Prevenar vaccination



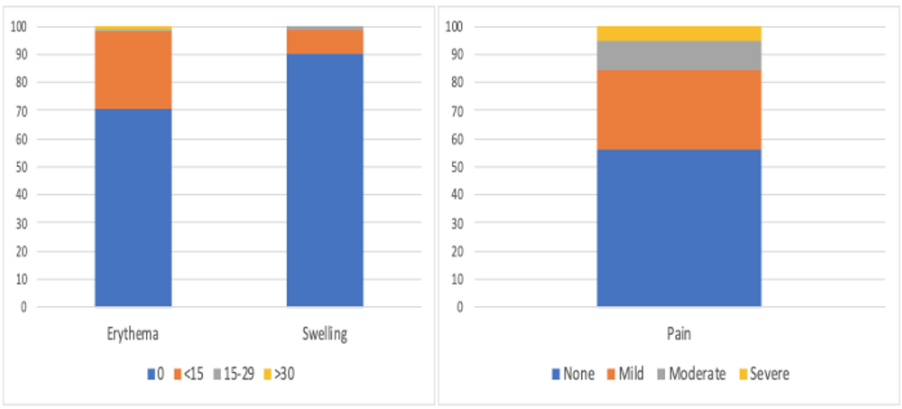
A: Erythema B: Swelling C: Tenderness

Figure 14: Graphs of local reactions experienced following Priorix vaccination



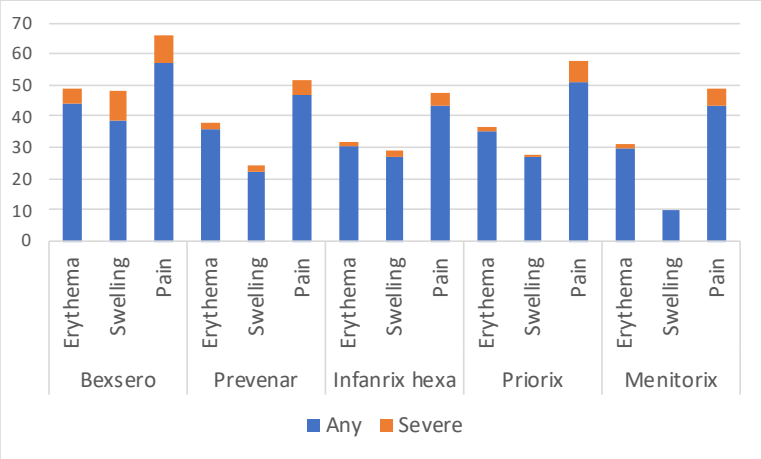
A: Erythema and swelling B: Tenderness

Figure 15: Graphs of local reactions experienced following Menitorix vaccination



A: Erythema and swelling B: Tenderness

Figure 16: Percentage of local reactions per dose of vaccine administered



Conclusions

This is the first study to investigate the immunogenicity of Bexsero in a preterm population. We were able to recruit a population of preterm infants with a wide range of gestational ages, of which 50% were very premature (<30 weeks). Our broad eligibility criteria means that this population is likely to be representative of the preterm population in the UK.

At five and twelve months of age, the proportion of infants with titres ≥1:4 against PorA was significantly higher in those who received the 3+1 schedule and this was reflected at five months of age in the GMTs against PorA in babies 30-34+6 weeks and at twelve months of age in all babies. At five months there was also a significant difference in GMTs against NadA, with the 3+1 schedule being superior, but there was no difference in proportions ≥1:4. At thirteen months, there were no differences seen in PorA GMTs, nor proportions ≥1:4, but there was a significant difference in fHbp for those babies born at less than 30 weeks, with titres being higher in the participants who received the 3+1 schedule, although this was not reflected in proportions ≥1:4.

We used a composite cut off of ≥1:4 to ≥2/3 tested antigens to make a decision about whether to offer a booster vaccination. When this cut off was used to compare between groups at the three assessed time points, there were no differences between groups at any time, but this probably reflects the high degree of response to NadA and fHbp. This may not necessarily correlate with vaccine effectiveness as protection at an individual level will depend on the titres at the time of exposure as well as the specific strain the individual is exposed to.

There are no differences in PorA between groups following booster vaccination. A recent study using a reduced 2+1 schedule in term infants has shown that proportions with a titre ≥1:4 following primary vaccination was lower for PorA than for the other antigens.(1) Of

note, the results obtained in this study for term infants are similar to those seen in our preterm population using a 3+1 schedule. Whilst preterm infants appear to be better protected against PorA expressing strains in their first year of life using a 3+1 schedule, the relevance of this for the effectiveness of the vaccine depends on the prevalence of strains which express PorA in the community. The reported MATS coverage immediately prior to the introduction of Bexsero showed that 16% of invasive strains expressed PorA, but in less than 1% was this the only expressed antigen and in 6% this was one of two expressed antigens.(2) There is a well-established surveillance programme in the UK which monitors cases of invasive meningococcal disease and would allow early identification of an increase in cases caused by PorA expressing strains. If such an increase was identified then a change of schedule (to 3+1) could be considered for preterm infants.

Interestingly, the post boost response for fHbp was slightly reduced compared to the post primary response in the reduced schedule group This has also been observed in term infants receiving a 2+1 schedule.(1) This might lead to speculation that a 2+1 schedule is less immunogenic for fHbp, although in our population even those who received a 3+1 schedule had a post boost response which was less than expected and only slightly greater than the post primary response.

There were a large number of SAEs reported in participants of this study which reflects the vulnerable nature of the preterm population. At visit 2, when babies in group 2 received an additional dose of Bexsero there was a statistically significant increase in fever reported within 7 days, but no increase in cardiorespiratory instability, no difference in fever reported within 28 days, no difference in rate of systemic reactions reported and no difference in investigations or treatment for sepsis. Investigation for sepsis and antibiotic treatment was most common following visit 1. Local reactions were common, particularly pain following Bexsero vaccination.

References

1. Davis K, Valente Pinto M, Andrews NJ, Goldblatt D, Borrow R, Findlow H, et al. Immunogenicity of the UK group B meningococcal vaccine (4CMenB) schedule against groups B and C meningococcal strains (Sched3): outcomes of a multicentre, open-label, randomised controlled trial. The Lancet Infectious Diseases. 2021.
2. Parikh SR, Newbold L, Slater S, Stella M, Moschioni M, Lucidarme J, et al. Meningococcal serogroup B strain coverage of the multicomponent 4CMenB vaccine with corresponding regional distribution and clinical characteristics in England, Wales, and Northern Ireland, 2007–08 and 2014–15: a qualitative and quantitative assessment. The Lancet Infectious Diseases. 2017;17(7):754-62.