Clinical trial results:
A multicentre, multinational, parallel group, observer-blind, randomised, placebo-controlled study on the Group B Streptococcus vaccine (GBS-NN/NN2), investigating the immunogenicity and safety of four vaccination regimens in pregnant woman, assessing IgG specific to AlpN proteins in cord blood and maternal blood, and the safety profile in mother and infant up to 6 months post-delivery

Summary

EudraCT number	2021-003214-40
Trial protocol	DK
Global end of trial date	18 October 2023

Results information

Result version number	v1 (current)
This version publication date	06 December 2024
First version publication date	06 December 2024

Trial information

Trial identification

Sponsor protocol code	MVX0004

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	MinervaX ApS
Sponsor organisation address	Nordre Fasanvej 215, Frederiksberg, Denmark, 2000
Public contact	Clinical Trials Information, MinervaX Aps, +45 39 17 82 82, lio@minervax.com
Scientific contact	Clinical Trials Information, MinervaX Aps, +45 39 17 82 82, lio@minervax.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	26 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 April 2023
Global end of trial reached?	Yes
Global end of trial date	18 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the concentrations of IgG specific to the AlpN proteins (RibN, Alp1N, Alp2N and AlpCN) in cord blood from babies, born to women who received the GBS-NN/NN2 vaccine or placebo, according to four vaccination regimens during pregnancy, between the GBS-NN/NN2 and placebo groups:
• Group 1: 2 doses GBS-NN/NN2 at 26 & 30 weeks GA
• Group 2: 2 doses GBS-NN/NN2 at 22 & 26 weeks GA
• Group 3: 2 doses GBS-NN/NN2 at 22 & 30 weeks GA
• Group 4: 1 dose GBS-NN/NN2 at 26 weeks GA
• Group 5: Placebo at 22, 26, and 30 weeks GA

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 59
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	South Africa: 195
Worldwide total number of subjects	269
EEA total number of subjects	59

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)	269
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first participant first visit took place on 17 February 2022 and the last participant last visit took place on 18 October 2023.

Pre-assignment

Screening details:

A total of 400 maternal participants signed the ICF and were enrolled in the study, of whom 272 were eligible and randomised to one of the 5 study groups (3 participants were randomised in error). Enrolment was stopped with 269 randomised participants who received at least one dose of the study vaccine or placebo.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: 4 week dose interval; 2 doses

Arm description:

Participants received one injection of placebo at 22 (±1) weeks GA (gestational age), one injection of GBS-NN/NN2 at 26 (±1) weeks GA and one injection of GBS- NN/NN2 at 30 (±1) weeks GA

Arm type	Experimental
Investigational medicinal product name	GBS-NN/NN2 Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL GBS-NN/NN2 containing 50 µg of GBS-NN and 50 µg of GBS-NN2 and 0.5 mg of aluminium, given by intramuscular injection

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

Dosage and administration details:

0.5 mL normal saline given by intramuscular injection

Arm title	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses

Arm description:

Participants received one injection of GBS-NN/NN2 at 22 (±1) weeks GA, one injection of GBS-NN/NN2 at 26 (±1) weeks GA and one injection of placebo at 30 (±1) weeks GA

Arm type	Experimental
Investigational medicinal product name	GBS-NN/NN2 Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL GBS-NN/NN2 containing 50 µg of GBS-NN and 50 µg of GBS-NN2 and 0.5 mg of aluminium, given by intramuscular injection

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

Dosage and administration details:

0.5 mL normal saline given by intramuscular injection

Arm title	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses

Arm description:

Participants received one injection of GBS-NN/NN2 at 22 (±1) weeks GA, one injection of placebo at 26 (±1) weeks GA and one injection of GBS- NN/NN2 at 30 (±1) weeks GA

Arm type	Experimental
Investigational medicinal product name	GBS-NN/NN2 Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL GBS-NN/NN2 containing 50 µg of GBS-NN and 50 µg of GBS-NN2 and 0.5 mg of aluminium, given by intramuscular injection

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

Dosage and administration details:

0.5 mL normal saline given by intramuscular injection

Arm title	Group 4: Single Dose

Arm description:

Participants received one injection of placebo at 22 (±1) weeks GA, one injection of GBS-NN/NN2 at 26 (±1) weeks GA, and one injection of placebo at 30 (±1) weeks GA.

Arm type	Experimental
Investigational medicinal product name	GBS-NN/NN2 Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL GBS-NN/NN2 containing 50 µg of GBS-NN and 50 µg of GBS-NN2 and 0.5 mg of aluminium, given by intramuscular injection

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

Dosage and administration details:

0.5 mL normal saline given by intramuscular injection

Arm title	Group 5: Placebo

Arm description:	
Participants received one injection of placebo at 22, 26 and 30 weeks (±1) GA	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL normal saline given by intramuscular injection

Number of subjects in period 1	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses
Started	61	59	59
Completed	59	54	56
Not completed	2	5	3
Consent withdrawn by subject	2	3	2
Adverse event, non-fatal	-	-	-
Baby loss	-	1	-
Lost to follow-up	-	1	-
Relocated to another province	-	-	1

Number of subjects in period 1	Group 4: Single Dose	Group 5: Placebo
Started	60	30
Completed	52	29
Not completed	8	1
Consent withdrawn by subject	4	-
Adverse event, non-fatal	1	-
Baby loss	-	-
Lost to follow-up	3	-
Relocated to another province	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: 4 week dose interval; 2 doses
Reporting group description:	
Participants received one injection of placebo at 22 (±1) weeks GA (gestational age), one injection of GBS-NN/NN2 at 26 (±1) weeks GA and one injection of GBS- NN/NN2 at 30 (±1) weeks GA	
Reporting group title	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses
Reporting group description:	
Participants received one injection of GBS-NN/NN2 at 22 (±1) weeks GA, one injection of GBS-NN/NN2 at 26 (±1) weeks GA and one injection of placebo at 30 (±1) weeks GA	
Reporting group title	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses
Reporting group description:	
Participants received one injection of GBS-NN/NN2 at 22 (±1) weeks GA, one injection of placebo at 26 (±1) weeks GA and one injection of GBS- NN/NN2 at 30 (±1) weeks GA	
Reporting group title	Group 4: Single Dose
Reporting group description:	
Participants received one injection of placebo at 22 (±1) weeks GA, one injection of GBS-NN/NN2 at 26 (±1) weeks GA, and one injection of placebo at 30 (±1) weeks GA.	

Reporting group title	Group 5: Placebo
Reporting group description:	
Participants received one injection of placebo at 22, 26 and 30 weeks (±1) GA	

Reporting group values	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses
Number of subjects	61	59	59
Age categorical 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)	61	59	59
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	28.9	27.5	27.8
standard deviation	± 5.26	± 4.81	± 5.34
Gender categorical Units: Subjects			
Female	61	59	59
Male	0	0	0

Region of Enrollment Units: Subjects			
Denmark	13	14	12
United Kingdom	4	3	4
South Africa	44	42	43
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	0	1
Not Hispanic or Latino	59	59	58
Height Units: cm			
arithmetic mean	161.7	162.2	163.3
standard deviation	± 7.84	± 8.00	± 7.58
Weight Units: kg			
arithmetic mean	71.1	73	73.6
standard deviation	± 14.00	± 12.11	± 14.52
BMI Units: kg/m^2			
arithmetic mean	27.2	27.9	27.6
standard deviation	± 5.28	± 5.32	± 5.35

Reporting group values	Group 4: Single Dose	Group 5: Placebo	Total
Number of subjects	60	30	269
Age categorical 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)	60	30	269
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	27.3	28.3	
standard deviation	± 5.37	± 6.65	-
Gender categorical Units: Subjects			
Female	60	30	269
Male	0	0	0
Region of Enrollment Units: Subjects			
Denmark	13	7	59
United Kingdom	3	1	15
South Africa	44	22	195
Ethnicity (NIH/OMB) Units: Subjects			

Hispanic or Latino	0	1	4
Not Hispanic or Latino	60	29	265

Height			
Units: cm			
arithmetic mean	160.5	160.5	
standard deviation	± 6.88	± 6.92	-
Weight			
Units: kg			
arithmetic mean	70.6	74.2	
standard deviation	± 14.59	± 13.38	-
BMI			
Units: kg/m^2			
arithmetic mean	27.5	28.8	
standard deviation	± 5.57	± 5.38	-

End points

End points reporting groups

Reporting group title	Group 1: 4 week dose interval; 2 doses
Reporting group description:	
Participants received one injection of placebo at 22 (±1) weeks GA (gestational age), one injection of GBS-NN/NN2 at 26 (±1) weeks GA and one injection of GBS- NN/NN2 at 30 (±1) weeks GA	
Reporting group title	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses
Reporting group description:	
Participants received one injection of GBS-NN/NN2 at 22 (±1) weeks GA, one injection of GBS-NN/NN2 at 26 (±1) weeks GA and one injection of placebo at 30 (±1) weeks GA	
Reporting group title	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses
Reporting group description:	
Participants received one injection of GBS-NN/NN2 at 22 (±1) weeks GA, one injection of placebo at 26 (±1) weeks GA and one injection of GBS- NN/NN2 at 30 (±1) weeks GA	
Reporting group title	Group 4: Single Dose
Reporting group description:	
Participants received one injection of placebo at 22 (±1) weeks GA, one injection of GBS-NN/NN2 at 26 (±1) weeks GA, and one injection of placebo at 30 (±1) weeks GA.	

Reporting group title	Group 5: Placebo
Reporting group description:	
Participants received one injection of placebo at 22, 26 and 30 weeks (±1) GA	

Primary: Concentrations of Immunoglobulin (Ig) G Antibodies Specific to the AlpN Proteins in µg/mL in Cord Blood From Each Baby

End point title	Concentrations of Immunoglobulin (Ig) G Antibodies Specific to the AlpN Proteins in µg/mL in Cord Blood From Each Baby
End point description:	
Concentrations of IgG antibodies specific to the AlpN proteins in µg/mL in cord blood from each baby at birth	
End point type	Primary
End point timeframe:	
Delivery	

End point values	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses	Group 4: Single Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59[1]	57[2]	56[3]	55[4]
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Alp1N	11.13 (± 239.4)	5.51 (± 169.7)	7.35 (± 238.2)	2.58 (± 730.1)
Alp2N	6.97 (± 326.5)	5.30 (± 282.3)	5.08 (± 377.4)	2.58 (± 740.2)
AlpCN	9.08 (± 236.9)	6.85 (± 311.7)	6.70 (± 369.2)	2.68 (± 691.3)
RibN	3.55 (± 224)	1.97 (± 418.7)	3.42 (± 258.3)	1.15 (± 601.0)

Notes:

[1] - Alp1N = 57, Alp2N = 52, AlpCN = 52, RibN = 54

[2] - Alp1N = 54, Alp2N = 50, AlpCN = 56, RibN = 53

[3] - Alp1N = 52, Alp2N = 50, AlpCN = 53, RibN = 54

[4] - Alp1N = 52, Alp2N = 53, AlpCN = 53, RibN = 54

End point values	Group 5: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Alp1N	0.08 (± 89.1)			
Alp2N	0.05 (± 126.2)			
AlpCN	0.08 (± 156.6)			
RibN	0.06 (± 125.5)			

Attachments (see zip file)	Primary endpoint statistical analysis.docx

Statistical analyses

Statistical analysis title	Analysis of primary immunogenicity endpoint

Statistical analysis description:

Group 1 was selected as the perceived standard and reference group, whereas Groups 2 and 3 each represent useful practical alternatives that are expected to perform on a comparable level. Group 4 represents a sub-optimal but still useful vaccination schedule that would be likely to occur in real life. Antibody concentrations for the 4 AlpN proteins were described through seroprotection levels (concentrations above 0.1, 0.2, 0.5, 1, 2, 4, and 8 µg/mL) and geometric mean concentrations (GMCs).

Comparison groups	Group 1: 4 week dose interval; 2 doses v Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses v Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses v Group 4: Single Dose v Group 5: Placebo
Number of subjects included in analysis	255
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	> 0.001 [6]
Method	Please see comment
Parameter estimate	Geometric mean
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.5
upper limit	97.5

Notes:

[5] - The non-inferiority hypotheses tests had margins of 15 percentage point difference on the absolute scale for the seroprotection and a ratio of 2/3 for the GMC. Non-inferiority tests were performed using a one-sided 5% significance level. Confidence intervals of the point estimates were reported using a two-sided 95% confidence level.

[6] - Method: Hypothesis tests for geometric mean ratios were based on one-sided t-tests on the log-transformed concentration ratios. The difference in seroprotection was tested using the Newcombe-Wilson method

*See attached table for p-value overview

Secondary: Injection Site Reactions in the Mother

End point title	Injection Site Reactions in the Mother

End point description:

Number of participants with solicited injection site reactions following vaccination

End point type	Secondary

End point timeframe:

7 days following each injection

End point values	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses	Group 4: Single Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	60
Units: participant				
Redness : 0 - 2.4 cm	7	5	9	5
Redness : 2.5 - 5.0 cm	2	1	2	0
Redness : 5.1 - 10.0 cm	0	1	0	0
Redness : >10 cm	0	0	0	0
Swelling : Palpable "firmness" only	14	10	9	6
Swelling : 0 - 2.4 cm	5	2	2	2
Swelling : 2.5 - 5.0 cm	0	2	0	0
Swelling : 5.1 - 10.0 cm	0	0	0	0
Tenderness: Mild	14	17	18	16
Tenderness: Moderate	15	12	13	10
Tenderness: Severe	0	0	1	0
Itching	23	20	15	14
Pain: Mild	35	35	34	24
Pain: Moderate	3	3	2	0
Pain: Severe	0	0	0	0

End point values	Group 5: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: participant				
Redness : 0 - 2.4 cm	5			
Redness : 2.5 - 5.0 cm	0			
Redness : 5.1 - 10.0 cm	0			
Redness : >10 cm	0			
Swelling : Palpable "firmness" only	1			
Swelling : 0 - 2.4 cm	0			
Swelling : 2.5 - 5.0 cm	0			
Swelling : 5.1 - 10.0 cm	0			
Tenderness: Mild	3			
Tenderness: Moderate	1			

Tenderness: Severe	0			
Itching	4			
Pain: Mild	3			
Pain: Moderate	0			
Pain: Severe	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse Events Following the Vaccinations in the Mother

End point title	Adverse Events Following the Vaccinations in the Mother

End point description:

Number of participants with solicited and other adverse events following the vaccinations

End point type	Secondary

End point timeframe:

To Day 84

End point values	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses	Group 4: Single Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	60
Units: Participants				
Number	56	54	57	56

End point values	Group 5: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Participants				
Number	26			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinically Significant Abnormal Laboratory Tests in the Mother

End point title	Clinically Significant Abnormal Laboratory Tests in the Mother

End point description:

Number of participants with clinically significant abnormal laboratory tests in the mother

End point type	Secondary

End point timeframe:

To Day 84

End point values	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses	Group 4: Single Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	60
Units: Participants				
Number	0	0	0	0

End point values	Group 5: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Participants				
Number	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinically Significant Changes in Vital Signs in the Mother

End point title	Clinically Significant Changes in Vital Signs in the Mother

End point description:

Number of participants with clinically significant changes in vital signs (heart rate, blood pressure, oral temperature) in
the mother

End point type	Secondary

End point timeframe:

To Day 84

End point values	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses	Group 4: Single Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	60
Units: Participants				
Number	0	0	0	0

End point values	Group 5: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Participants				
Number	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinically Significant Changes in Physical Examination in the Mother

End point title	Clinically Significant Changes in Physical Examination in the Mother

End point description:

Number of participants with clinically significant changes in physical examination in the mother

End point type	Secondary

End point timeframe:

To Day 84

End point values	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses	Group 4: Single Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	60
Units: Participants				
Number	0	0	0	0

End point values	Group 5: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	30			

Units: Participants				
Number	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Gestational Age

End point title	Gestational Age
End point description: Gestational age at birth	
End point type	Secondary
End point timeframe: Delivery	

End point values	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses	Group 4: Single Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	60
Units: Age (months)				
arithmetic mean (standard deviation)				
Age	38.7 (± 2.88)	38.9 (± 2.39)	38.9 (± 2.30)	38.8 (± 2.37)

End point values	Group 5: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Age (months)				
arithmetic mean (standard deviation)				
Age	39.4 (± 1.45)			

Statistical analyses

No statistical analyses for this end point

Secondary: Weight of the Baby

End point title	Weight of the Baby

End point description:
Weight of the baby

End point type	Secondary

End point timeframe:
Delivery

End point values	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses	Group 4: Single Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	60
Units: Grams				
arithmetic mean (standard deviation)				
Weight of the Baby	3165.4 (± 585.45)	3086.5 (± 679.5)	3230.1 (± 638.71)	2955.3 (± 598.35)

End point values	Group 5: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Grams				
arithmetic mean (standard deviation)				
Weight of the Baby	3272.4 (± 629.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Length of the Baby

End point title	Length of the Baby

End point description:
Length of the baby

End point type	Secondary

End point timeframe:
Delivery

End point values	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses	Group 4: Single Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	60
Units: centimeters				
arithmetic mean (standard deviation)				
Length of the baby	50.3 (± 3.59)	49.9 (± 2.96)	49.3 (± 4.88)	48.9 (± 4.42)

End point values	Group 5: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: centimeters				
arithmetic mean (standard deviation)				
Length of the baby	49.7 (± 4.45)			

Statistical analyses

No statistical analyses for this end point

Secondary: Head Circumference of the Baby

End point title	Head Circumference of the Baby
End point description: Head Circumference of the Baby	
End point type	Secondary
End point timeframe: Delivery	

End point values	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses	Group 4: Single Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	60
Units: centimetre				
arithmetic mean (standard deviation)				
Head Circumference of the Baby	34.4 (± 1.83)	34.3 (± 1.68)	33.8 (± 2.49)	34.0 (± 2.19)

End point values	Group 5: Placebo			

Subject group type	Reporting group			
Number of subjects analysed	30			
Units: centimetre				
arithmetic mean (standard deviation)				
Head Circumference of the Baby	34.8 (± 1.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apgar Score in the Baby

End point title	Apgar Score in the Baby

End point description:

Apgar score in the baby (Appearance; Pulse; Grimace response; Activity; Respiration).
Range 0 to 10 where high scores are good and low scores are bad.

End point type	Secondary

End point timeframe:

1, 5 and 10 minutes

End point values	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses	Group 4: Single Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	60
Units: Score on a scale				
arithmetic mean (standard deviation)				
APGAR score at 1 minute	8.8 (± 1.39)	9.0 (± 0.91)	8.8 (± 1.00)	8.9 (± 1.38)
APGAR score at 5 minutes	9.7 (± 1.34)	9.8 (± 0.54)	9.8 (± 0.60)	9.9 (± 0.32)
APGAR score at 10 minutes	9.9 (± 0.29)	9.9 (± 0.28)	9.9 (± 0.33)	9.9 (± 0.29)

End point values	Group 5: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Score on a scale				
arithmetic mean (standard deviation)				
APGAR score at 1 minute	8.8 (± 1.22)			
APGAR score at 5 minutes	9.8 (± 0.62)			
APGAR score at 10 minutes	10.0 (± 0.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of IgG Antibodies Specific to the AlpN Proteins in µg/mL in Maternal Blood

End point title	Concentrations of IgG Antibodies Specific to the AlpN Proteins in µg/mL in Maternal Blood

End point description:

Concentrations of IgG Antibodies Specific to the AlpN Proteins in µg/mL in Maternal Blood

End point type	Secondary

End point timeframe:

Delviery

End point values	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses	Group 4: Single Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[7]	52[8]	54[9]	55[10]
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Alp1N	40.57 (± 271)	15.81 (± 295.1)	32.91 (± 322.2)	12.38 (± 604.4)
Alp2N	61.69 (± 384.9)	32.74 (± 275.1)	39.54 (± 239.9)	18.96 (± 491.4)
AlpCN	48.11 (± 314.7)	25.17 (± 328.6)	27.53 (± 332.7)	16.38 (± 482.6)
RibN	25.55 (± 323.2)	10.97 (± 305.5)	20.08 (± 473.4)	8.68 (± 614.4)

Notes:

[7] - Alp1N 56, Alp2N 56, AlpCN 58, RibN 56

[8] - Alp1N 48, Alp2N 45, AlpCN 52, RibN 51

[9] - Alp1N 54, Alp2N 49, AlpCN 54, RibN 52

[10] - Alp1N 52, Alp2N 47, AlpCN 51, RibN 55

End point values	Group 5: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	27[11]			
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Alp1N	1.03 (± 85.3)			
Alp2N	1.02 (± 95.9)			
AlpCN	1.10 (± 86.4)			
RibN	0.92 (± 74.4)			

Notes:

[11] - Alp1N 27, Alp2N 28, AlpCN 27, RibN 23

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of IgG Antibodies Specific to the AlpN Proteins in µg/mL in Blood From Each Baby

End point title	Concentrations of IgG Antibodies Specific to the AlpN Proteins in µg/mL in Blood From Each Baby

End point description:

1 month, 3 months

End point type	Secondary

End point timeframe:

Concentrations of IgG Antibodies Specific to the AlpN Proteins in µg/mL in Blood From Each Baby

End point values	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses	Group 4: Single Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[12]	54[13]	52[14]	60[15]
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Alp1N: At 1 month of age	5.60 (± 423.9)	3.23 (± 193.4)	6.43 (± 117.4)	1.42 (± 1441.5)
Alp1N: At 3 month of age	1.84 (± 361.9)	1.39 (± 155.6)	2.00 (± 161.1)	0.58 (± 455.4)
Alp2N: At 1 month of age	4.62 (± 348.2)	3.22 (± 274.4)	3.5585 (± 250.2)	1.42 (± 712.5)
Alp2N: At 3 month of age	1.69 (± 268.7)	1.14 (± 251.3)	1.19 (± 244.8)	0.60 (± 505)
AlpCN: At 1 month of age	5.27 (± 431.2)	3.94 (± 257.3)	4.1634 (± 398.7)	1.37 (± 1359.0)
AlpCN: At 3 month of age	1.73 (± 354.3)	1.36 (± 301.0)	1.54 (± 217.4)	0.58 (± 431.9)
RibN: At 1 month of age	2.48 (± 249.1)	1.37 (± 233)	2.20 (± 221.3)	0.64 (± 769.9)
RibN: At 3 month of age	0.78 (± 282.2)	0.54 (± 223.2)	0.77 (± 230.4)	0.25 (± 354.7)

Notes:

[12] - 55, 58, 51, 50, 55, 58, 55, 58 respectively

[13] - 54, 51, 51, 44, 53, 51, 54, 51 respectively

[14] - 49, 52, 46, 46, 51, 52, 51, 52 respectively

[15] - 51, 48, 49, 40, 51, 48, 51, 48 respecitvely

End point values	Group 5: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	30[16]			
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Alp1N: At 1 month of age	0.05 (± 316.9)			
Alp1N: At 3 month of age	0.03 (± 106.4)			
Alp2N: At 1 month of age	0.05 (± 384.8)			
Alp2N: At 3 month of age	0.02 (± 111.8)			

AlpCN: At 1 month of age	0.07 (± 335.5)			
AlpCN: At 3 month of age	0.04 (± 116)			
RibN: At 1 month of age	0.05 (± 212)			
RibN: At 3 month of age	0.03 (± 85.7)			

Notes:

[16] - 27, 28, 28, 28, 28, 28, 28, 28

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TAES in the mother were assessed from the time of informed consent sign-off until Day 84 (Visit 7). From delivery (Visit 8) onwards, only Medically attended adverse events (MAAEs), Adverse events of special interest (AESIs) and SAEs were assessed.

Adverse event reporting additional description:

Solicited local and systemic reactions were collected in electronic diaries up to 7 days following each administered vaccination. In addition, other AEs, i.e., unsolicited AEs, including MAAEs, SAEs, concomitant medication or vaccines were to be recorded in the electronic diary.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Group 1: 4 week dose interval; 2 doses

Reporting group description:

Participants received one injection of placebo at 22 (±1) weeks GA (gestational age), one injection of GBS-NN/NN2 at 26 (±1) weeks GA and one injection of GBS- NN/NN2 at 30 (±1) weeks GA

Reporting group title	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses

Reporting group description:

Participants received one injection of GBS-NN/NN2 at 22 (±1) weeks GA, one injection of GBS-NN/NN2 at 26 (±1) weeks GA and one injection of placebo at 30 (±1) weeks GA

Reporting group title	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses

Reporting group description:

Participants received one injection of GBS-NN/NN2 at 22 (±1) weeks GA, one injection of placebo at 26 (±1) weeks GA and one injection of GBS- NN/NN2 at 30 (±1) weeks GA

Reporting group title	Group 4: Single Dose

Reporting group description:

Participants received one injection of placebo at 22 (±1) weeks GA, one injection of GBS-NN/NN2 at 26 (±1) weeks GA, and one injection of placebo at 30 (±1) weeks GA.

Reporting group title	Group 5: Placebo

Reporting group description:

Participants received one injection of placebo at 22, 26 and 30 weeks (±1) GA

Serious adverse events	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 61 (37.70%)	12 / 59 (20.34%)	20 / 59 (33.90%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypertension			

subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive emergency			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Artificial rupture of membranes			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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
Abortion threatened			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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
Amniorrhoea			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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
Cephalo-pelvic disproportion			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failed induction of labour			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

False labour			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal growth restriction			
subjects affected / exposed	1 / 61 (1.64%)	1 / 59 (1.69%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal death			
subjects affected / exposed	2 / 61 (3.28%)	1 / 59 (1.69%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal distress syndrome			
subjects affected / exposed	8 / 61 (13.11%)	2 / 59 (3.39%)	5 / 59 (8.47%)
occurrences causally related to treatment / all	0 / 8	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal hypokinesia			
subjects affected / exposed	0 / 61 (0.00%)	2 / 59 (3.39%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal macrosomia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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
Foetal vascular malperfusion			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gestational hypertension			
subjects affected / exposed	2 / 61 (3.28%)	1 / 59 (1.69%)	4 / 59 (6.78%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gestational diabetes			

subjects affected / exposed	2 / 61 (3.28%)	0 / 59 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HELLP syndrome			
subjects affected / exposed	2 / 61 (3.28%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage in pregnancy			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intrapartum haemorrhage			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large for dates baby			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meconium in amniotic fluid			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oligohydramnios			
subjects affected / exposed	2 / 61 (3.28%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Placenta praevia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Placental insufficiency			

subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postpartum haemorrhage			
subjects affected / exposed	2 / 61 (3.28%)	2 / 59 (3.39%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pre-eclampsia			
subjects affected / exposed	3 / 61 (4.92%)	3 / 59 (5.08%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Premature delivery			
subjects affected / exposed	1 / 61 (1.64%)	3 / 59 (5.08%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Premature labour			
subjects affected / exposed	0 / 61 (0.00%)	2 / 59 (3.39%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Premature rupture of membranes			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Premature separation of placenta			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prolonged labour			
subjects affected / exposed	3 / 61 (4.92%)	1 / 59 (1.69%)	3 / 59 (5.08%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prolonged pregnancy			

subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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
Prolonged rupture of membranes			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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
Retroplacental haematoma			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine hypotonus			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Vaginal discharge			
subjects affected / exposed	1 / 61 (1.64%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Foetal monitoring abnormal			

subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Perineal injury			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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
Cardiac disorders			
Bradycardia foetal			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	1 / 61 (1.64%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Headache			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 61 (3.28%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 61 (1.64%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Amniotic cavity infection			
subjects affected / exposed	1 / 61 (1.64%)	1 / 59 (1.69%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial vaginosis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Beta haemolytic streptococcal infection			

subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometritis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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
Escherichia infection			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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
Gastroenteritis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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
Postoperative wound infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postpartum sepsis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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
Pyelonephritis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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
Upper respiratory tract infection			
subjects affected / exposed	1 / 61 (1.64%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 61 (1.64%)	4 / 59 (6.78%)	5 / 59 (8.47%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 59 (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

Serious adverse events	Group 4: Single Dose	Group 5: Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 60 (41.67%)	14 / 30 (46.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Surgical and medical procedures			
Artificial rupture of membranes			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion threatened			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amniorrhoea			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cephalo-pelvic disproportion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failed induction of labour			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
False labour			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal growth restriction			
subjects affected / exposed	4 / 60 (6.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Foetal death			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal distress syndrome			
subjects affected / exposed	12 / 60 (20.00%)	7 / 30 (23.33%)	
occurrences causally related to treatment / all	0 / 12	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal hypokinesia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal macrosomia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal vascular malperfusion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gestational hypertension			
subjects affected / exposed	4 / 60 (6.67%)	3 / 30 (10.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gestational diabetes			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HELLP syndrome			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage in pregnancy			

subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intrapartum haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large for dates baby			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meconium in amniotic fluid			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oligohydramnios			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Placenta praevia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Placental insufficiency			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postpartum haemorrhage			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pre-eclampsia			

subjects affected / exposed	4 / 60 (6.67%)	2 / 30 (6.67%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature delivery			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature labour			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature rupture of membranes			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature separation of placenta			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prolonged labour			
subjects affected / exposed	3 / 60 (5.00%)	2 / 30 (6.67%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prolonged pregnancy			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prolonged rupture of membranes			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroplacental haematoma			

subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine hypotonus			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Vaginal discharge			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Foetal monitoring abnormal			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Perineal injury			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			

subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Bradycardia foetal			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Amniotic cavity infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial vaginosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Beta haemolytic streptococcal infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometritis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia infection			

subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postpartum sepsis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection enterococcal			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Group 1: 4 week dose interval; 2 doses	Group 2: Early Intervention; 4 Week Dose Interval; 2 Doses	Group 3: Early Intervention; 8 Week Dose Interval; 2 Doses
Total subjects affected by non-serious adverse events			
subjects affected / exposed	56 / 61 (91.80%)	54 / 59 (91.53%)	57 / 59 (96.61%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 61 (3.28%)	3 / 59 (5.08%)	1 / 59 (1.69%)
occurrences (all)	2	3	2
Blood pressure increased			
subjects affected / exposed	3 / 61 (4.92%)	2 / 59 (3.39%)	4 / 59 (6.78%)
occurrences (all)	3	3	4
C-reactive protein increased			
subjects affected / exposed	0 / 61 (0.00%)	2 / 59 (3.39%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 61 (3.28%)	0 / 59 (0.00%)	4 / 59 (6.78%)
occurrences (all)	2	0	5
Nervous system disorders			

Dizziness			
subjects affected / exposed	2 / 61 (3.28%)	3 / 59 (5.08%)	0 / 59 (0.00%)
occurrences (all)	2	3	0
Headache			
subjects affected / exposed	8 / 61 (13.11%)	7 / 59 (11.86%)	5 / 59 (8.47%)
occurrences (all)	8	9	5
Pregnancy, puerperium and perinatal conditions			
Foetal hypokinesia			
subjects affected / exposed	4 / 61 (6.56%)	4 / 59 (6.78%)	7 / 59 (11.86%)
occurrences (all)	5	6	7
Gestational hypertension			
subjects affected / exposed	2 / 61 (3.28%)	2 / 59 (3.39%)	4 / 59 (6.78%)
occurrences (all)	2	2	4
Prolonged pregnancy			
subjects affected / exposed	1 / 61 (1.64%)	3 / 59 (5.08%)	1 / 59 (1.69%)
occurrences (all)	1	3	1
Uterine contractions during pregnancy			
subjects affected / exposed	4 / 61 (6.56%)	1 / 59 (1.69%)	1 / 59 (1.69%)
occurrences (all)	4	1	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 61 (4.92%)	4 / 59 (6.78%)	3 / 59 (5.08%)
occurrences (all)	3	4	3
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 61 (1.64%)	4 / 59 (6.78%)	0 / 59 (0.00%)
occurrences (all)	1	4	0
Influenza like illness			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	3 / 59 (5.08%)
occurrences (all)	1	0	3
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	3 / 59 (5.08%)
occurrences (all)	0	0	3
Abdominal pain upper			

subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	4 / 59 (6.78%)
occurrences (all)	0	0	4
Diarrhoea			
subjects affected / exposed	6 / 61 (9.84%)	2 / 59 (3.39%)	2 / 59 (3.39%)
occurrences (all)	7	2	2
Dyspepsia			
subjects affected / exposed	2 / 61 (3.28%)	4 / 59 (6.78%)	6 / 59 (10.17%)
occurrences (all)	2	5	6
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	2 / 59 (3.39%)
occurrences (all)	1	0	2
Nausea			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	1 / 61 (1.64%)	1 / 59 (1.69%)	3 / 59 (5.08%)
occurrences (all)	1	1	3
Reproductive system and breast disorders			
Vaginal discharge			
subjects affected / exposed	5 / 61 (8.20%)	5 / 59 (8.47%)	3 / 59 (5.08%)
occurrences (all)	6	5	5
Vaginal haemorrhage			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	4 / 59 (6.78%)
occurrences (all)	1	0	4
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	3 / 61 (4.92%)	1 / 59 (1.69%)	4 / 59 (6.78%)
occurrences (all)	3	1	5
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	3 / 59 (5.08%)
occurrences (all)	0	1	3
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	2 / 61 (3.28%)	1 / 59 (1.69%)	3 / 59 (5.08%)
occurrences (all)	2	1	5
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 61 (1.64%)	4 / 59 (6.78%)	1 / 59 (1.69%)
occurrences (all)	1	5	1
Streptococcal urinary tract infection			
subjects affected / exposed	0 / 61 (0.00%)	2 / 59 (3.39%)	3 / 59 (5.08%)
occurrences (all)	0	2	3
Upper respiratory tract infection			
subjects affected / exposed	9 / 61 (14.75%)	5 / 59 (8.47%)	9 / 59 (15.25%)
occurrences (all)	10	5	9
Urinary tract infection			
subjects affected / exposed	15 / 61 (24.59%)	13 / 59 (22.03%)	8 / 59 (13.56%)
occurrences (all)	17	16	9
Vulvovaginal candidiasis			
subjects affected / exposed	3 / 61 (4.92%)	2 / 59 (3.39%)	2 / 59 (3.39%)
occurrences (all)	3	3	2

Non-serious adverse events	Group 4: Single Dose	Group 5: Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	56 / 60 (93.33%)	26 / 30 (86.67%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Blood pressure increased			
subjects affected / exposed	1 / 60 (1.67%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
C-reactive protein increased			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	
occurrences (all)	3	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 60 (1.67%)	3 / 30 (10.00%)	
occurrences (all)	2	3	

Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Headache			
subjects affected / exposed	4 / 60 (6.67%)	4 / 30 (13.33%)	
occurrences (all)	4	8	
Pregnancy, puerperium and perinatal conditions			
Foetal hypokinesia			
subjects affected / exposed	2 / 60 (3.33%)	3 / 30 (10.00%)	
occurrences (all)	4	3	
Gestational hypertension			
subjects affected / exposed	1 / 60 (1.67%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Prolonged pregnancy			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Uterine contractions during pregnancy			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	
occurrences (all)	4	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 60 (3.33%)	3 / 30 (10.00%)	
occurrences (all)	2	3	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			

subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Dyspepsia			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	3	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 60 (3.33%)	3 / 30 (10.00%)	
occurrences (all)	2	3	
Nausea			
subjects affected / exposed	1 / 60 (1.67%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Vomiting			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Reproductive system and breast disorders			
Vaginal discharge			
subjects affected / exposed	4 / 60 (6.67%)	1 / 30 (3.33%)	
occurrences (all)	4	3	
Vaginal haemorrhage			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	0 / 60 (0.00%)	4 / 30 (13.33%)	
occurrences (all)	0	4	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	3	1	
Streptococcal urinary tract infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	6 / 60 (10.00%)	5 / 30 (16.67%)	
occurrences (all)	7	6	
Urinary tract infection			
subjects affected / exposed	14 / 60 (23.33%)	7 / 30 (23.33%)	
occurrences (all)	16	8	
Vulvovaginal candidiasis			
subjects affected / exposed	6 / 60 (10.00%)	3 / 30 (10.00%)	
occurrences (all)	6	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 September 2021	MVX0004 Protocol Version 2.0 This protocol update was issued prior to study start to include a new investigational site in the UK (Site 4). In addition, the following main changes were made: • Addition of exclusion criterion #24 "The pregnancy was considered high risk by treating physicians" based on regulatory authority feedback. • Clarification of procedures for maintaining the blind during injections of vaccine/placebo, based on regulatory authority feedback. • Clarification that MAAEs, AESIs, SAEs and related concomitant medications were to be recorded for mothers and infants throughout the study until 6 months after delivery and that this would be checked 28 days post each vaccination, based on regulatory authority feedback. • Clarification that the investigational vaccine would be assembled either by the site pharmacy or by unblinded trained nursing staff. • Clarification of the randomisation procedure • Clarification of assessments of laboratory values indicating "liver injury", including seriousness criteria. • Specification of the use of the FDA toxicity grading scale based on regulatory authority feedback. • Inclusion of safety monitoring by the DSMB based on regulatory authority feedback. • Clarification and change in wording of halting rules for the study based on regulatory authority feedback. • Specification of the "Estimand".
21 November 2021	MVX0004 Protocol Version 3.0 This protocol update was issued prior to study start. The main changes were as follows based on regulatory authority feedback: • Ensure safety laboratory testing within 28 days pre-vaccination(s), and within 3-5 days post vaccination(s). • Update of the amount of blood taken from mothers up to 215 mL, due to implementation of the extra safety blood tests. • Clarification and change in wording of halting rules for the study based on regulatory authority feedback.
08 April 2022	This protocol update was issued after study start. The main changes were as follows: • Update of the time window for vital signs, urinalysis, immunogenicity blood sample and collection of breast milk (colostrum) sample from maternal participants from within 48 hours to within 72 hours of delivery to better comply with clinical practice. The samechange was made for the immunogenicity blood sample for infant participants. • Inclusion of South Africa as study country to ensure recruitment. • Revision of the GA for the vaccination schedule to clarify the intended dose regimens and avoid misinterpretations of the visit windows in the study schedule. • Update of the time window for participant inclusion to reflect the intended dose regimen as the first dose administered during GA 22 (22+0 – 22+6) ± 1 week. • Revision of the visit windows to allow increased flexibility in visit windows

14 April 2023	This protocol update was issued after study start to include an interim analysis of study data for the primary and key secondary endpoints available up to 72 hours after delivery (Visit 8). This analysis was added to inform decisions on the design of a long-term follow-up study as well as the vaccination regimens to be administered in Phase III studies. Interim analysis of these data would allow to advance the clinical development plan for the GBS-NN/NN2 vaccine and was expected to address the unmet medical need for GBS vaccination during pregnancy.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported