Clinical trial results:
Vitamin D And Lifestyle Intervention for Gestational Diabetes Mellitus (GDM) Prevention - A European multicentre, randomised trial: Vitamin D limb.

Summary

EudraCT number	2013-000789-13
Trial protocol	AT BE
Global end of trial date	31 January 2016

Results information

Result version number	v1 (current)
This version publication date	04 September 2016
First version publication date	04 September 2016

Trial information

Trial identification

Sponsor protocol code	Trial_version1

Additional study identifiers

ISRCTN number	ISRCTN70595832
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	VU University Medical Center
Sponsor organisation address	van der Boechorststraat 7, Amsterdam, Netherlands, 1081 BT
Public contact	Trial Coordinator, Cambridge University Hospitals NHS Foundation Trust, +61 246203899, da.simmons@westernsydney.edu.au
Scientific contact	Trial Coordinator, Cambridge University Hospitals NHS Foundation Trust, +61 246203899, da.simmons@westernsydney.edu.au

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	31 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 January 2016
Global end of trial reached?	Yes
Global end of trial date	31 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1) To identify the best available measures to prevent GDM in an ongoing pregnancy
2) Comparison of the impact of increased physical activity, enhanced nutrition and Vitamin D supplementation either alone or in combination on maternal glucose tolerance, maternal weight gain and insulin sensitivity

Protection of trial subjects:

Before inclusion and during the intervention, participants were screened for hypercalciuria (≥2.27 mmol/mmol calcium/creatinine) and hypercalcaemia (at 24–28 weeks >9.0 mg/dl | 2.25 mmol/l; and at 35–37 weeks > 9.7 mg/dl |2.43 mmol/l). With blood levels exceeding these values, the intervention was stopped.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2013
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	Austria: 25
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Italy: 22
Country: Number of subjects enrolled	United Kingdom: 41
Country: Number of subjects enrolled	Ireland: 15
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	Poland: 20
Worldwide total number of subjects	154
EEA total number of subjects	154

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)	154
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment took place in 7 European countries (United Kingdom, Ireland, Austria, Poland, Italy (Padua, Pisa), Spain, and Belgium) from March 2013-July 2015.

Pre-assignment

Screening details:

Screening for existing GDM using IADPSG/WHO 2013 criteria (fasting venous plasma glucose ≥ 5.1 mmol/l and/or 1 hour glucose ≥10 mmol/l and/or 2 hour glucose ≥ 8.5 mmol/l).

Period 1

Period 1 title	< 20 weeks of gestation
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Healthy eating and physical activity and placebo

Arm description:

Women received 5 face-to-face and up to 4 telephone coaching sessions on healty eating and physical activity, based on the principles of motivational interviewing. In addition, placebo tablets identical to the vitamin D tablets.

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0 IU per tablet. Participants are requested to take 4 tablets per day.

Arm title	Vitamin D

Arm description:

1600 IU/day vitamin D in tablet form: Devaron®, produced by Vemedia (Diemen, Netherlands) (RVG 09766)

Arm type	Experimental
Investigational medicinal product name	vitamin D
Investigational medicinal product code	A11CC05
Other name	Devaron
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Taking into account that most women use multivitamins during pregnancy, containing on average 400 IU vitamin D, we chose to use a dosage of 1600 IU/day as the intervention dosage in our trial, in tablet form, Devaron®, produced by Vemedia (Diemen, Netherlands) (RVG 09766). Each tablet contains 400 IU, and participants are asked to take 4 tablets/day until delivery.
Devaron is prepacked in bottles containing 90 tablets each.

Arm title	vitaminD&HE&PA

Arm description:

vitamin D (1600 IU/day) as in Arm 2 combined with counseling on healthy eating (HE) and physcial activity (PA) as in Arm 1.

Arm type	Active comparator
Investigational medicinal product name	vitamin D
Investigational medicinal product code	A11CC05
Other name	Devaron
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Taking into account that most women use multivitamins during pregnancy, containing on average 400 IU vitamin D, we chose to use a dosage of 1600 IU/day as the intervention dosage in our trial, in tablet form, Devaron®, produced by Vemedia (Diemen, Netherlands) (RVG 09766). Each tablet contains 400 IU, and participants are asked to take 4 tablets/day until delivery.
Devaron is prepacked in bottles containing 90 tablets each.

Arm title	Placebo

Arm description:

Placebo tablets identical to the vitamin D tablets

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0 IU per tablet. Participants are requested to take 4 tablets per day.

Number of subjects in period 1	Healthy eating and physical activity and placebo	Vitamin D	vitaminD&HE&PA
Started	38	42	37
Completed	38	42	37

Number of subjects in period 1	Placebo
Started	37
Completed	37

Period 2

Period 2 title	24-28 weeks of gestation
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes

Arm title	Healthy eating and physical activity and placebo

Arm description:

Women received 5 face-to-face and up to 4 telephone coaching sessions on healty eating and physical activity, based on the principles of motivational interviewing. In addition, placebo tablets identical to the vitamin D tablets.

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0 IU per tablet. Participants are requested to take 4 tablets per day.

Arm title	Vitamin D

Arm description:

1600 IU/day vitamin D in tablet form: Devaron®, produced by Vemedia (Diemen, Netherlands) (RVG 09766)

Arm type	Experimental
Investigational medicinal product name	vitamin D
Investigational medicinal product code	A11CC05
Other name	Devaron
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Taking into account that most women use multivitamins during pregnancy, containing on average 400 IU vitamin D, we chose to use a dosage of 1600 IU/day as the intervention dosage in our trial, in tablet form, Devaron®, produced by Vemedia (Diemen, Netherlands) (RVG 09766). Each tablet contains 400 IU, and participants are asked to take 4 tablets/day until delivery.
Devaron is prepacked in bottles containing 90 tablets each.

Arm title	vitaminD&HE&PA

Arm description:

vitamin D (1600 IU/day) as in Arm 2 combined with counseling on healthy eating (HE) and physcial activity (PA) as in Arm 1.

Arm type	Active comparator
Investigational medicinal product name	vitamin D
Investigational medicinal product code	A11CC05
Other name	Devaron
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Taking into account that most women use multivitamins during pregnancy, containing on average 400 IU vitamin D, we chose to use a dosage of 1600 IU/day as the intervention dosage in our trial, in tablet form, Devaron®, produced by Vemedia (Diemen, Netherlands) (RVG 09766). Each tablet contains 400 IU, and participants are asked to take 4 tablets/day until delivery.
Devaron is prepacked in bottles containing 90 tablets each.

Arm title	Placebo

Arm description:

Placebo tablets identical to the vitamin D tablets

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0 IU per tablet. Participants are requested to take 4 tablets per day.

Number of subjects in period 2	Healthy eating and physical activity and placebo	Vitamin D	vitaminD&HE&PA
Started	38	42	37
Completed	32	42	35
Not completed	6	0	2
Consent withdrawn by subject	1	-	-
Study takes too much time	4	-	-
miscarriage	-	-	1
Lost to follow-up	1	-	1

Number of subjects in period 2	Placebo
Started	37
Completed	34
Not completed	3
Consent withdrawn by subject	-
Study takes too much time	1
miscarriage	1
Lost to follow-up	1

Period 3	
Period 3 title	35-37 weeks of gestation
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms	
Are arms mutually exclusive?	Yes

Arm title	Healthy eating and physical activity and placebo

Arm description:

Women received 5 face-to-face and up to 4 telephone coaching sessions on healty eating and physical activity, based on the principles of motivational interviewing. In addition, placebo tablets identical to the vitamin D tablets.

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0 iU per tablet. Participants are requested to take 4 tablets per day.

Arm title	Vitamin D

Arm description:

1600 IU/day vitamin D in tablet form: Devaron®, produced by Vemedia (Diemen, Netherlands) (RVG 09766)

Arm type	Experimental
Investigational medicinal product name	vitamin D
Investigational medicinal product code	A11CC05
Other name	Devaron
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Taking into account that most women use multivitamins during pregnancy, containing on average 400 IU vitamin D, we chose to use a dosage of 1600 IU/day as the intervention dosage in our trial, in tablet form, Devaron®, produced by Vemedia (Diemen, Netherlands) (RVG 09766). Each tablet contains 400 IU, and participants are asked to take 4 tablets/day until delivery.
Devaron is prepacked in bottles containing 90 tablets each.

Arm title	vitaminD&HE&PA

Arm description:

vitamin D (1600 IU/day) as in Arm 2 combined with counseling on healthy eating (HE) and physcial activity (PA) as in Arm 1.

Arm type	Active comparator
Investigational medicinal product name	vitamin D
Investigational medicinal product code	A11CC05
Other name	Devaron
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Taking into account that most women use multivitamins during pregnancy, containing on average 400 IU vitamin D, we chose to use a dosage of 1600 IU/day as the intervention dosage in our trial, in tablet form, Devaron®, produced by Vemedia (Diemen, Netherlands) (RVG 09766). Each tablet contains 400 IU, and participants are asked to take 4 tablets/day until delivery.
Devaron is prepacked in bottles containing 90 tablets each.

Arm title	Placebo

Arm description:

Placebo tablets identical to the vitamin D tablets

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0 IU per tablet. Participants are requested to take 4 tablets per day.

Number of subjects in period 3	Healthy eating and physical activity and placebo	Vitamin D	vitaminD&HE&PA
Started	32	42	35
Completed	28	37	32
Not completed	4	5	3
unknown	2	-	-
Adverse event, non-fatal	-	-	-
Lost to follow-up	2	5	3

Number of subjects in period 3	Placebo
Started	34
Completed	31
Not completed	3
unknown	-
Adverse event, non-fatal	1
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Healthy eating and physical activity and placebo
Reporting group description:	
Women received 5 face-to-face and up to 4 telephone coaching sessions on healty eating and physical activity, based on the principles of motivational interviewing. In addition, placebo tablets identical to the vitamin D tablets.	
Reporting group title	Vitamin D
Reporting group description:	
1600 IU/day vitamin D in tablet form: Devaron®, produced by Vemedia (Diemen, Netherlands) (RVG 09766)	
Reporting group title	vitaminD&HE&PA
Reporting group description:	
vitamin D (1600 IU/day) as in Arm 2 combined with counseling on healthy eating (HE) and physcial activity (PA) as in Arm 1.	
Reporting group title	Placebo
Reporting group description:	
Placebo tablets identical to the vitamin D tablets	

Reporting group values	Healthy eating and physical activity and placebo	Vitamin D	vitaminD&HE&PA
Number of subjects	38	42	37
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Age at recruitment			
Units: years			
arithmetic mean	33.1	31.8	33
standard deviation	± 5.3	± 5.1	± 5.4
Gender categorical Units: Subjects			
Female	38	42	37
Male	0	0	0
Multiparous			
Women had a previous baby			
Units: Subjects			
Nulliparous	15	23	15
Multiparous	23	19	22

Reporting group values	Placebo	Total	
Number of subjects	37	154	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Age at recruitment			
Units: years			
arithmetic mean	32.5		
standard deviation	± 5.6	-	
Gender categorical Units: Subjects			
Female	37	154	
Male	0	0	
Multiparous			
Women had a previous baby			
Units: Subjects			
Nulliparous	17	70	
Multiparous	20	84	

End points

End points reporting groups

Reporting group title	Healthy eating and physical activity and placebo
Reporting group description:	
Women received 5 face-to-face and up to 4 telephone coaching sessions on healty eating and physical activity, based on the principles of motivational interviewing. In addition, placebo tablets identical to the vitamin D tablets.	
Reporting group title	Vitamin D
Reporting group description:	
1600 IU/day vitamin D in tablet form: Devaron®, produced by Vemedia (Diemen, Netherlands) (RVG 09766)	
Reporting group title	vitaminD&HE&PA
Reporting group description:	
vitamin D (1600 IU/day) as in Arm 2 combined with counseling on healthy eating (HE) and physcial activity (PA) as in Arm 1.	
Reporting group title	Placebo
Reporting group description:	
Placebo tablets identical to the vitamin D tablets	
Reporting group title	Healthy eating and physical activity and placebo
Reporting group description:	
Women received 5 face-to-face and up to 4 telephone coaching sessions on healty eating and physical activity, based on the principles of motivational interviewing. In addition, placebo tablets identical to the vitamin D tablets.	
Reporting group title	Vitamin D
Reporting group description:	
1600 IU/day vitamin D in tablet form: Devaron®, produced by Vemedia (Diemen, Netherlands) (RVG 09766)	
Reporting group title	vitaminD&HE&PA
Reporting group description:	
vitamin D (1600 IU/day) as in Arm 2 combined with counseling on healthy eating (HE) and physcial activity (PA) as in Arm 1.	
Reporting group title	Placebo
Reporting group description:	
Placebo tablets identical to the vitamin D tablets	
Reporting group title	Healthy eating and physical activity and placebo
Reporting group description:	
Women received 5 face-to-face and up to 4 telephone coaching sessions on healty eating and physical activity, based on the principles of motivational interviewing. In addition, placebo tablets identical to the vitamin D tablets.	
Reporting group title	Vitamin D
Reporting group description:	
1600 IU/day vitamin D in tablet form: Devaron®, produced by Vemedia (Diemen, Netherlands) (RVG 09766)	
Reporting group title	vitaminD&HE&PA
Reporting group description:	
vitamin D (1600 IU/day) as in Arm 2 combined with counseling on healthy eating (HE) and physcial activity (PA) as in Arm 1.	
Reporting group title	Placebo
Reporting group description:	
Placebo tablets identical to the vitamin D tablets	

Primary: Gestational weight gain

End point title	Gestational weight gain

End point description:

Maternal gestational weight gain isbe defined as the weight change from baseline measurement to the last measurement at 35–37 weeks of gestation.

End point type	Primary

End point timeframe:

35-37 weeks

End point values	Healthy eating and physical activity and placebo	Vitamin D	vitaminD&HE&PA	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	37	33	32
Units: kg				
arithmetic mean (standard deviation)	7.78 (± 4.25)	7.42 (± 4.74)	8.43 (± 5.17)	8.09 (± 7.33)

Statistical analyses

Statistical analysis title	Factorial weight gain

Statistical analysis description:

Both vitamin D arms were combined and compared with the combined placebo groups, regardless of lifestyle intervention (using the factorial design) since no interaction was present between the two intervention modalities.

Comparison groups	Placebo v Healthy eating and physical activity and placebo v Vitamin D v vitaminD&HE&PA
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Slope
Point estimate	-1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.66
upper limit	0.6

Primary: Fasting glucose

End point title	Fasting glucose

End point description:

End point type	Primary

End point timeframe:
24-28 weeks

End point values	Healthy eating and physical activity and placebo	Vitamin D	vitaminD&HE&PA	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	42	33[1]	33[2]
Units: mmol/l				
arithmetic mean (standard deviation)	4.76 (± 0.53)	4.57 (± 0.41)	4.67 (± 0.38)	4.64 (± 0.44)

Notes:
[1] - No blood sample from 3 women
[2] - no blood sample from one woman

Statistical analyses

Statistical analysis title	Factorial fasting glucose
Comparison groups	Healthy eating and physical activity and placebo v Vitamin D v vitaminD&HE&PA v Placebo
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Slope
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.04

Primary: Insulin sensitivity

End point title	Insulin sensitivity

End point description:

End point type	Primary

End point timeframe:
24-28 weeks

End point values	Healthy eating and physical activity and placebo	Vitamin D	vitaminD&HE&PA	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	42	33[3]	33[4]
Units: HOMA index				
median (inter-quartile range (Q1-Q3))	2.83 (2.03 to 4.5)	2.85 (2.27 to 4.16)	3.11 (2.22 to 4.01)	2.88 (2.08 to 4.07)

Notes:

[3] - OGTT not succesful in 2 women

[4] - OGTT not succesful in one woman

Statistical analyses

Statistical analysis title	Factorial HOMA

Statistical analysis description:

Both vitamin D arms were combined and compared with the two combined placebo groups, regardless of lifestyle intervention (using the factorial design) since no interaction was present between the two intervention modalities.

Comparison groups	Placebo v Healthy eating and physical activity and placebo v Vitamin D v vitaminD&HE&PA
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Slope
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.21

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From baseline till 7 days after delivery	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups	
Reporting group title	Healthy eating and physical activity and placebo
Reporting group description: Women received 5 face-to-face and up to 4 telephone coaching sessions on healty eating and physical activity, based on the principles of motivational interviewing. In addition, placebo tablets identical to the vitamin D tablets.	
Reporting group title	Vitamin D
Reporting group description: 1600 IU/day vitamin D in tablet form: Devaron®, produced by Vemedia (Diemen, Netherlands) (RVG 09766)	
Reporting group title	vitaminD&HE&PA
Reporting group description: vitamin D (1600 IU/day) as in Arm 2 combined with counseling on healthy eating (HE) and physcial activity (PA) as in Arm 1.	
Reporting group title	Placebo
Reporting group description: Placebo tablets identical to the vitamin D tablets	

Serious adverse events	Healthy eating and physical activity and placebo	Vitamin D	vitaminD&HE&PA
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 38 (5.26%)	3 / 42 (7.14%)	2 / 37 (5.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Congenital, familial and genetic disorders			
Large vessel transposition			
subjects affected / exposed	0 / 38 (0.00%)	0 / 42 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal atresia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 42 (2.38%)	0 / 37 (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

Vascular disorders			
High blood pressure	Additional description: Hospitalisation for 5 days with raised blood pressure		
subjects affected / exposed	0 / 38 (0.00%)	1 / 42 (2.38%)	0 / 37 (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
Pregnancy, puerperium and perinatal conditions			
miscarriage			
subjects affected / exposed	0 / 38 (0.00%)	0 / 42 (0.00%)	0 / 37 (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
blood loss	Additional description: Hospitalised for 7 days with unstable lie and had PPH of 1500 mls at LSCS.		
subjects affected / exposed	0 / 38 (0.00%)	0 / 42 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Maternal fever	Additional description: Suspected neonatal sepsis after maternal fever during labour		
subjects affected / exposed	1 / 38 (2.63%)	0 / 42 (0.00%)	0 / 37 (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	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 37 (2.70%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Congenital, familial and genetic disorders			
Large vessel transposition			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal atresia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			

High blood pressure	Additional description: Hospitalisation for 5 days with raised blood pressure		
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
miscarriage			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
blood loss	Additional description: Hospitalised for 7 days with unstable lie and had PPH of 1500 mls at LSCS.		
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Maternal fever	Additional description: Suspected neonatal sepsis after maternal fever during labour		
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Healthy eating and physical activity and placebo	Vitamin D	vitaminD&HE&PA
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 38 (34.21%)	25 / 42 (59.52%)	20 / 37 (54.05%)
Vascular disorders			
Pregnancy induced hypertension			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 38 (2.63%)	6 / 42 (14.29%)	3 / 37 (8.11%)
occurrences (all)	1	6	3
Pregnancy, puerperium and perinatal conditions			
Caesarean section			
alternative assessment type: Systematic			

subjects affected / exposed	12 / 38 (31.58%)	19 / 42 (45.24%)	17 / 37 (45.95%)
occurrences (all)	12	19	17

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 37 (48.65%)		
Vascular disorders			
Pregnancy induced hypertension			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Pregnancy, puerperium and perinatal conditions			
Caesarean section			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 37 (43.24%)		
occurrences (all)	16		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported