Clinical trial results:
A phase 2, double-blind, dose-finding, placebo-controlled study to assess the safety and efficacy of a single oral administration of OBE001 to improve embryo implantation following IVF or ICSI.

Summary

EudraCT number	2014-002254-40
Trial protocol	GB BE DK CZ ES PL
Global end of trial date	29 November 2016

Results information

Result version number	v1 (current)
This version publication date	17 December 2017
First version publication date	17 December 2017

Trial information

Trial identification

Sponsor protocol code	14-OBE001-013

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	ObsEva SA
Sponsor organisation address	12, Chemin des Aulx, Plan-Les Ouates, Geneva, Switzerland, 1228
Public contact	Véronique Lecomte, ObsEva SA, +41 225521550, clinicaltrials@obseva.ch
Scientific contact	Véronique Lecomte, ObsEva SA, +41 225521550, clinicaltrials@obseva.ch

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	05 July 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 November 2016
Global end of trial reached?	Yes
Global end of trial date	29 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Efficacy, to:
• Assess efficacy of a range of single oral doses of OBE001 compared to placebo to increase the clinical pregnancy rate defined as a positive embryo heart-beat at 6 weeks post Embryo Transfer (ET) day.

Safety, to:
• Evaluate safety + tolerability of OBE001 when administered orally to women undergoing ET following IVF or ICSI.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles of the International Conference on Harmonisation (ICH) Guidelines on Good Clinical Practice (GCP), the Declaration of Helsinki and all other applicable local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 January 2015
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	Poland: 68
Country: Number of subjects enrolled	Spain: 37
Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	Czech Republic: 104
Country: Number of subjects enrolled	Denmark: 27
Worldwide total number of subjects	247
EEA total number of subjects	247

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)	247
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Four hundred and thirty (430) subjects were screened for participation in this study

Pre-assignment

Screening details:

183 subjects (43%) were screening failures.

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	Investigator, Monitor, Data analyst, Carer, Assessor, Subject

Blinding implementation details:

Prior to the start of the study, a randomisation list was generated by the designated statistician and transmitted to the assigned clinical packaging organization for labelling and to a fully web-integrated IWR system. The randomisation list +/or the electronic file was secured in a locked cabinet +/or an electronic file with access restricted to only the designated personnel directly responsible for labelling + handling study medication until study database was locked and ready to be unblinded

Arms

Are arms mutually exclusive?	Yes
Arm title	placebo

Arm description:

placebo to match

The mean (SD) number of oocytes retrieved in the placebo group was 11.0 (5.2)
The mean (SD) number of embryos obtained in the placebo group was 6.6 (3.1)

Arm type	Placebo
Investigational medicinal product name	placebo to match
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

2 x placebo 50 mg tablets and
4 x placebo 200 mg tablets
were administered as a single oral dose at the investigational site on the day of the embryo transfer, 4 hours (±1hr) prior to the embryo transfer.

Immediately prior to administration, the six tablets were dispersed in half a glass of plain water (approximately 125 ml) until a completely homogeneous dispersion was obtained and then swallowed. Afterwards, the container was rinsed with plain water and the rinsing water swallowed. A container made of glass and not of plastic was recommended.

Arm title	100mg OBE001

Arm description:

100mg OBE001

The mean (SD) number of oocytes retrieved in the 100 mg group was 10.3 (4.4)
The mean (SD) number of embryos obtained in the 100 mg group was 6.2 (3.7)

Arm type	Experimental

Investigational medicinal product name	100mg OBE001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

2 x 50 mg OBE001 tablets and
4 x placebo 200 mg tablets
were administered as a single oral dose at the investigational site on the day of the embryo transfer, 4 hours (±1hr) prior to the embryo transfer.

Immediately prior to administration, the six tablets were dispersed in half a glass of plain water (approximately 125 ml) until a completely homogeneous dispersion was obtained and then swallowed. Afterwards, the container was rinsed with plain water and the rinsing water swallowed. A container made of glass and not of plastic was recommended.

Arm title	300mg OBE001

Arm description:

300mg OBE001

The demographic characteristics were generally comparable between the treatment groups. However there was an indication of slightly more oocytes retrieved and embryos obtained in the 300 mg group.
The mean (SD) number of oocytes retrieved in the 300 mg group was 11.7 (5.6).
The mean (SD) number of embryos obtained in the 300 mg group was 7.3 (4.1).

There was also an indication that levels of P4 and E2 measured at baseline were higher in the 300 mg group.

Arm type	Experimental
Investigational medicinal product name	300mg OBE001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

2 x 50 mg OBE001 tablets and
1 x 200 mg OBE001 tablet and
3 x placebo 200 mg tablets
were administered as a single oral dose at the investigational site on the day of the embryo transfer, 4 hours (±1hr) prior to the embryo transfer.

Immediately prior to administration, the six tablets were dispersed in half a glass of plain water (approximately 125 ml) until a completely homogeneous dispersion was obtained and then swallowed. Afterwards, the container was rinsed with plain water and the rinsing water swallowed. A container made of glass and not of plastic was recommended.

Arm title	900mg OBE001

Arm description:

900mg OBE001

The mean (SD) number of oocytes retrieved in the 900 mg group was 10.2 (4.1).
The mean (SD) number of embryos obtained in the 900 mg group was 5.9 (3.2).

Arm type	Experimental
Investigational medicinal product name	900mg OBE001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

2 x 50 mg OBE001 tablets and
4 x 200mg OBE001 tablets
were administered as a single oral dose at the investigational site on the day of the embryo transfer, 4 hours (±1hr) prior to the embryo transfer.

Immediately prior to administration, the six tablets were dispersed in half a glass of plain water (approximately 125 ml) until a completely homogeneous dispersion was obtained and then swallowed. Afterwards, the container was rinsed with plain water and the rinsing water swallowed. A container made of glass and not of plastic was recommended.

Number of subjects in period 1	placebo	100mg OBE001	300mg OBE001
Started	65	62	60
Completed	64	61	60
Not completed	1	1	0
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	-	-	-
Lost to follow-up	-	1	-

Number of subjects in period 1	900mg OBE001
Started	60
Completed	59
Not completed	1
Consent withdrawn by subject	-
Adverse event, non-fatal	1
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	placebo
Reporting group description: placebo to match The mean (SD) number of oocytes retrieved in the placebo group was 11.0 (5.2) The mean (SD) number of embryos obtained in the placebo group was 6.6 (3.1)	
Reporting group title	100mg OBE001
Reporting group description: 100mg OBE001 The mean (SD) number of oocytes retrieved in the 100 mg group was 10.3 (4.4) The mean (SD) number of embryos obtained in the 100 mg group was 6.2 (3.7)	
Reporting group title	300mg OBE001
Reporting group description: 300mg OBE001 The demographic characteristics were generally comparable between the treatment groups. However there was an indication of slightly more oocytes retrieved and embryos obtained in the 300 mg group. The mean (SD) number of oocytes retrieved in the 300 mg group was 11.7 (5.6). The mean (SD) number of embryos obtained in the 300 mg group was 7.3 (4.1). There was also an indication that levels of P4 and E2 measured at baseline were higher in the 300 mg group.	
Reporting group title	900mg OBE001
Reporting group description: 900mg OBE001 The mean (SD) number of oocytes retrieved in the 900 mg group was 10.2 (4.1). The mean (SD) number of embryos obtained in the 900 mg group was 5.9 (3.2).	

Reporting group values	placebo	100mg OBE001	300mg OBE001
Number of subjects	65	62	60
Age categorical			
The subject was a healthy female volunteer aged from 18 years to 36 years inclusive at screening.			
Units: Subjects			
Adults (18-64 years)	65	62	60
Age continuous			
The subject was a healthy female volunteer aged from 18 years to 36 years inclusive at screening.			
Units: years			
arithmetic mean	31.5	31.5	31.8
full range (min-max)	24 to 36	25 to 36	24 to 36
Gender categorical			
Units: Subjects			
Female	65	62	60
Mean progesterone levels measured at baseline (Safety Set)			
Serum progesterone (P4) levels were measured at baseline (visit 2).			
Units: nmol/l			
arithmetic mean	287.67	256.65	321.93
standard deviation	± 156.58	± 155.11	± 155.42

Reporting group values	900mg OBE001	Total	
Number of subjects	60	247	
Age categorical			
The subject was a healthy female volunteer aged from 18 years to 36 years inclusive at screening.			
Units: Subjects			
Adults (18-64 years)	60	247	
Age continuous			
The subject was a healthy female volunteer aged from 18 years to 36 years inclusive at screening.			
Units: years			
arithmetic mean	31.1		
full range (min-max)	23 to 36	-	
Gender categorical			
Units: Subjects			
Female	60	247	
Mean progesterone levels measured at baseline (Safety Set)			
Serum progesterone (P4) levels were measured at baseline (visit 2).			
Units: nmol/l			
arithmetic mean	238.71		
standard deviation	± 130.17	-	

Subject analysis sets

Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who received study medication. Subjects were analysed according to treatment randomised. This is the primary analysis set for the efficacy analyses.

Subject analysis set title	post hoc OBE001 pooled
Subject analysis set type	Full analysis

Subject analysis set description:

Pooled subjects in the FAS population who received OBE001
Of 182 subjects who received OBE001:
62 received OBE001 100 mg,
60 received 300 mg and
60 received 900 mg

Subject analysis set title	post hoc placebo excl sbjcts in top Q of pre-dose P4
Subject analysis set type	Sub-group analysis

Subject analysis set description:

post hoc placebo excluding subjects in top Quartile of pre-dose P4

Subject analysis set title	post hoc OBE001 100mg excl sbjcts in top Q of pre-dose P4
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Analysis of the pregnancy endpoints was repeated after excluding subjects in the top quartile of the pre-dose P4

Subject analysis set title	post hoc OBE001 300mg excl sbjcts in top Q of pre-dose P4
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Analysis of the pregnancy endpoints was repeated after excluding subjects in the top quartile of the pre-dose P4

Subject analysis set title	post hoc OBE001 900mg excl sbjcts in top Q of pre-dose P4
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Analysis of the pregnancy endpoints was repeated after excluding subjects in the top quartile of the pre-dose P4

Reporting group values	Full analysis set (FAS)	post hoc OBE001 pooled	post hoc placebo excl sbjcts in top Q of pre-dose P4
Number of subjects	247	182	49
Age categorical			
The subject was a healthy female volunteer aged from 18 years to 36 years inclusive at screening.			
Units: Subjects			
Adults (18-64 years)	247		
Age continuous			
The subject was a healthy female volunteer aged from 18 years to 36 years inclusive at screening.			
Units: years			
arithmetic mean	31.4		
full range (min-max)	23 to 36		
Gender categorical			
Units: Subjects			
Female	247		
Mean progesterone levels measured at baseline (Safety Set)			
Serum progesterone (P4) levels were measured at baseline (visit 2).			
Units: nmol/l			
arithmetic mean			
standard deviation	±	±	±

Reporting group values	post hoc OBE001 100mg excl sbjcts in top Q of pre-dose P4	post hoc OBE001 300mg excl sbjcts in top Q of pre-dose P4	post hoc OBE001 900mg excl sbjcts in top Q of pre-dose P4
Number of subjects	50	35	49
Age categorical			
The subject was a healthy female volunteer aged from 18 years to 36 years inclusive at screening.			
Units: Subjects			
Adults (18-64 years)			
Age continuous			
The subject was a healthy female volunteer aged from 18 years to 36 years inclusive at screening.			
Units: years			
arithmetic mean			
full range (min-max)			
Gender categorical			
Units: Subjects			
Female			
Mean progesterone levels measured at baseline (Safety Set)			
Serum progesterone (P4) levels were measured at baseline (visit 2).			
Units: nmol/l			
arithmetic mean			
standard deviation	±	±	±

End points

End points reporting groups

Reporting group title	placebo

Reporting group description:

placebo to match

The mean (SD) number of oocytes retrieved in the placebo group was 11.0 (5.2)
The mean (SD) number of embryos obtained in the placebo group was 6.6 (3.1)

Reporting group title	100mg OBE001

Reporting group description:

100mg OBE001

The mean (SD) number of oocytes retrieved in the 100 mg group was 10.3 (4.4)
The mean (SD) number of embryos obtained in the 100 mg group was 6.2 (3.7)

Reporting group title	300mg OBE001

Reporting group description:

300mg OBE001

The demographic characteristics were generally comparable between the treatment groups. However there was an indication of slightly more oocytes retrieved and embryos obtained in the 300 mg group.
The mean (SD) number of oocytes retrieved in the 300 mg group was 11.7 (5.6).
The mean (SD) number of embryos obtained in the 300 mg group was 7.3 (4.1).

There was also an indication that levels of P4 and E2 measured at baseline were higher in the 300 mg group.

Reporting group title	900mg OBE001

Reporting group description:

900mg OBE001

The mean (SD) number of oocytes retrieved in the 900 mg group was 10.2 (4.1).
The mean (SD) number of embryos obtained in the 900 mg group was 5.9 (3.2).

Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who received study medication. Subjects were analysed according to treatment randomised. This is the primary analysis set for the efficacy analyses.

Subject analysis set title	post hoc OBE001 pooled
Subject analysis set type	Full analysis

Subject analysis set description:

Pooled subjects in the FAS population who received OBE001
Of 182 subjects who received OBE001:
62 received OBE001 100 mg,
60 received 300 mg and
60 received 900 mg

Subject analysis set title	post hoc placebo excl sbjcts in top Q of pre-dose P4
Subject analysis set type	Sub-group analysis

Subject analysis set description:

post hoc placebo excluding subjects in top Quartile of pre-dose P4

Subject analysis set title	post hoc OBE001 100mg excl sbjcts in top Q of pre-dose P4
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Analysis of the pregnancy endpoints was repeated after excluding subjects in the top quartile of the pre-dose P4

Subject analysis set title	post hoc OBE001 300mg excl sbjcts in top Q of pre-dose P4
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Analysis of the pregnancy endpoints was repeated after excluding subjects in the top quartile of the pre-dose P4

Subject analysis set title	post hoc OBE001 900mg excl sbjcts in top Q of pre-dose P4
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Analysis of the pregnancy endpoints was repeated after excluding subjects in the top quartile of the pre-dose P4

Primary: intra-uterine pregnancy with positive embryo heart-beat at 6 weeks post ET day (FAS)

End point title	intra-uterine pregnancy with positive embryo heart-beat at 6 weeks post ET day (FAS)

End point description:

Percentage of women with an intra-uterine pregnancy with positive embryo heart-beat at 6 weeks post ET day. The clinical pregnancy rate was:
33.8% (22/65) in placebo grp
46.8% (29/62) in 100 mg grp (p 0.151)
35.0% (21/60) in 300 mg grp and (p 1.000)
46.7% (28/60) in 900 mg grp (p 0.150)
When each OBE001 treatment grp was compared to the placebo grp individually no statistically significant differences were observed. These results were confirmed in the PP Set + in the FAS subgroup analysis. The results of the further exploratory analyses for the primary efficacy endpoint via logistic regression models generally confirmed the primary analysis although statistical significance was reached when fitting logistic regression model II (with treatment, site + embryo transfer rate as covariates) for the 100 mg grp compared to placebo (p-values = 0.093, 0.079 and 0.070 for the FAS, PP set + FAS subgroup respectively). The 900 mg grp cf to placebo also approached statistical significance.

End point type	Primary

End point timeframe:

6 weeks post Embryo Transfer day

End point values	placebo	100mg OBE001	300mg OBE001	900mg OBE001
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	62	60	60
Units: No. of women with +ve embryo heart beat				
Positive Embryo heart beat - YES	22	29	21	28
Positive Embryo heart beat - NO	43	33	39	32

Statistical analyses

Statistical analysis title	Cochran-Armitage test

Statistical analysis description:

The primary analysis of the primary endpoint tested the null hypothesis of no treatment effect against the ordered alternative and assessed via the Cochran-Armitage test of a linear trend in proportions
The percentage of subjects in each OBE001 treatment group was also compared to those in the placebo group via Fisher’s exact test

Comparison groups	placebo v 100mg OBE001 v 300mg OBE001 v 900mg OBE001

Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.33 [2]
Method	Cochran-Armitage test of a linear trend

Notes:

[1] - A two-sided type I error rate of 0.1 (corresponding to a one-sided type I error rate of 0.05) was used for the analysis of this phase 2 study.
[2] - When the % of subjects in each OBE001 treatment group was compared to those in the placebo group via Fisher's exact test, the resulting p-values were 0.151, 1.000 and 0.150 for the 100mg, 300mg and 900mg groups versus the placebo group respectively

Statistical analysis title	Clin Pregn rate Logistic Mod I - (FAS)

Statistical analysis description:

Analysis is based on a logistic model with PRIMARY ENDPOINT as dependent variable and Treatment as a continuous independent variable.
Comparison between individual doses was obtained using Treatment as a categorical variable.

Comparison groups	placebo v 100mg OBE001 v 300mg OBE001 v 900mg OBE001
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.308 [4]
Method	Regression, Logistic

Notes:

[3] - Logistic regression model with dose as a covariate

[4] - Fitting dose as a continuous effect (from 0 to 900) gave a p=0.308 when testing whether the slope was zero or not. Fitting dose as a categorical effect gave a p=0.274 when testing whether there were any differences between the four treatment groups

Statistical analysis title	Clin Pregn rate Logistic Mod I - 100mg v placebo

Statistical analysis description:

Comparison between individual doses was obtained using Treatment as a categorical variable.

Comparison groups	placebo v 100mg OBE001
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.139
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.72
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.94
upper limit	3.13

Notes:

[5] - Logistic regression model with dose as a covariate

Statistical analysis title	Clin Pregn rate Logistic Mod I - 300mg v placebo

Statistical analysis description:

Comparison between individual doses was obtained using Treatment as a categorical variable.

Comparison groups	placebo v 300mg OBE001

Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.892
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.05
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.57
upper limit	1.96

Notes:

[6] - Logistic regression model with dose as a covariate

Statistical analysis title	Clin Pregn rate Logistic Mod I - 900mg v placebo

Statistical analysis description:

Comparison between individual doses was obtained using Treatment as a categorical variable.

Comparison groups	placebo v 900mg OBE001
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.145
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.71
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.93
upper limit	3.13

Notes:

[7] - Logistic regression model with dose as a covariate

Statistical analysis title	Clin Pregn rate Logistic Mod II- (FAS)

Statistical analysis description:

Analysis is based on a logistic model with PRIMARY ENDPOINT as dependent variable and Treatment, Site and ETr (embryo transfer rate) as independent variables.

Analysis only includes subjects from sites with 4 or more subjects (in order to prevent quasi-complete separation; in exploratory fashion,as reported in SAP amendment 2).
No. of subjects=234.
No. of subjects considered in model =233

Comparison between individual doses was obtained using Treatment as a categorical variable.

Comparison groups	placebo v 100mg OBE001 v 300mg OBE001 v 900mg OBE001

Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	= 0.288 [9]
Method	Regression, Logistic

Notes:

[8] - Logistic regression model with dose as a covariate

[9] - p-value for independent variables:
CONTINUOUS DOSE - Treatment (Tx) 0.288, Site 0.844 + ETr 0.265;
CATEGORICAL DOSE -Tx 0.153, Site 0.823 + ETr 0.296.
Interaction (Tx*ETr) term p=0.968 for categorical dose model (excluded from model as >0.1)

Statistical analysis title	Clin Pregn rate Logistic Mod II- 100mg v placebo

Statistical analysis description:

Comparison between individual doses was obtained using Treatment as a categorical variable.

Comparison groups	placebo v 100mg OBE001
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	= 0.093 [11]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.94
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.01
upper limit	3.72

Notes:

[10] - Logistic regression model with dose as a covariate

[11] - Interaction (Tx*ETr) term p=0.968 for categorical dose model (excluded from model as >0.1)

Statistical analysis title	Clin Pregn rate Logistic Mod II- 300mg v placebo

Statistical analysis description:

Comparison between individual doses was obtained using Treatment as a categorical variable.

Comparison groups	placebo v 300mg OBE001
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	= 0.989 [13]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.99
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.51
upper limit	1.94

Notes:

[12] - Logistic regression model with dose as a covariate

[13] - Interaction (Tx*ETr) term p=0.968 for categorical dose model (excluded from model as >0.1)

Statistical analysis title	Clin Pregn rate Logistic Mod II- 900mg v placebo

Statistical analysis description:

Comparison between individual doses was obtained using Treatment as a categorical variable.

Comparison groups	placebo v 900mg OBE001
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	other[14]
P-value	= 0.116 [15]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.87
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.97
upper limit	3.59

Notes:

[14] - Logistic regression model with dose as a covariate

[15] - Interaction (Tx*ETr) term p=0.968 for categorical dose model (excluded from model as >0.1)

Post-hoc: Post hoc Positive embryo heart beat at 6 wk post Embryo Transfer day POOLED

End point title	Post hoc Positive embryo heart beat at 6 wk post Embryo Transfer day POOLED[16]

End point description:

End point type	Post-hoc

End point timeframe:

6 weeks post Embryo Transfer day

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Post hoc analysis comparing pooled OBE001 treatment arms versus placebo

End point values	placebo	post hoc OBE001 pooled		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	65	182		
Units: Number of women	22	78		

Statistical analyses

Statistical analysis title	Posthoc +ve embryo hrtbeat 6 wk post ET day POOLED

Statistical analysis description:

When all three active treatment groups were combined and compared to the placebo group, the positive pregnancy results for the placebo group and the pooled OBE001 treatment group at the endpoint at 6

weeks post ET were 33.8% and 42.9%.

Comparison groups	placebo v post hoc OBE001 pooled
Number of subjects included in analysis	247
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.24
Method	Fisher exact

Post-hoc: Post hoc Live birth (FAS) - POOLED

End point title	Post hoc Live birth (FAS) - POOLED[17]

End point description:

The endpoint "women with a live birth at end of pregnancy" was reported as positive for subjects where the outcome of pregnancy was equal to "delivery" on the Pregnancy Outcome and Neonatal Health form, otherwise the endpoint was reported as negative.

End point type	Post-hoc

End point timeframe:

women with a live birth at end of pregnancy

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Post hoc analysis comparing pooled OBE001 treatment arms versus placebo

End point values	placebo	post hoc OBE001 pooled		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	65	182		
Units: Number of women	19	72		

Statistical analyses

Statistical analysis title	Post hoc live birth (FAS)

Statistical analysis description:

Live birth at end of pregnancy

Comparison groups	placebo v post hoc OBE001 pooled
Number of subjects included in analysis	247
Analysis specification	Post-hoc
Analysis type	other[18]
P-value	= 0.177
Method	Fisher exact

Notes:

[18] - When all three active treatment groups were combined and compared to the placebo group, the positive pregnancy results for the placebo group and the pooled OBE001 treatment group at the endpoint for live birth were 29.2% and 39.6% respectively.

Post-hoc: Posthoc +ve embryo HB at wk 10 post OPU day (FAS excluding top quartile pre-dose P4) POOLED

End point title	Posthoc +ve embryo HB at wk 10 post OPU day (FAS excluding top quartile pre-dose P4) POOLED

End point description:

When the analyses were repeated after excluding subjects in the top pre-dose P4 quartile, the pregnancy results for the placebo group and the pooled active treatment group were 30.6% and 47.0% at 10 weeks post OPU.

End point type	Post-hoc

End point timeframe:

week 10 post Oocyte Pick Up (OPU) day

End point values	post hoc OBE001 pooled	post hoc placebo excl sbjcts in top Q of pre-dose P4		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	49	134		
Units: Number of women	15	63		

Statistical analyses

Statistical analysis title	Posthoc +ve embryo heartbeat at 10wks post OPU day

Statistical analysis description:

Full Analysis Set excluding subjects in the top pre-dose P4 quartile

Comparison groups	post hoc OBE001 pooled v post hoc placebo excl sbjcts in top Q of pre-dose P4
Number of subjects included in analysis	183
Analysis specification	Post-hoc
Analysis type	other[19]
P-value	= 0.063
Method	Fisher exact

Notes:

[19] - The analyses were repeated after excluding subjects in the top pre-dose P4 quartile

Post-hoc: Posthoc +ve embryo HB at wk 10 post OPU day (FAS excluding top quartile pre-dose P4)

End point title	Posthoc +ve embryo HB at wk 10 post OPU day (FAS excluding top quartile pre-dose P4)

End point description:

End point type	Post-hoc

End point timeframe:

Positive embryo Heart-Beat at week 10 post Oocyte Pick-Up (OPU) day

End point values	post hoc placebo excl sbjcts in top Q of pre-dose P4	post hoc OBE001 100mg excl sbjcts in top Q of pre-dose P4	post hoc OBE001 300mg excl sbjcts in top Q of pre-dose P4	post hoc OBE001 900mg excl sbjcts in top Q of pre-dose P4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	49	50	35	49
Units: Number of women	15	21	17	25

Statistical analyses

Statistical analysis title	Post hoc +ve embryo HB at wk 10 post OPU day
Comparison groups	post hoc placebo excl sbjcts in top Q of pre-dose P4 v post hoc OBE001 100mg excl sbjcts in top Q of pre-dose P4 v post hoc OBE001 300mg excl sbjcts in top Q of pre-dose P4 v post hoc OBE001 900mg excl sbjcts in top Q of pre-dose P4
Number of subjects included in analysis	183
Analysis specification	Post-hoc
Analysis type	other[20]
P-value	= 0.035 [21]
Method	Cochran-Armitage trend test

Notes:

[20] - Pregnancy rates increased with increasing dose for the pregnancy endpoints at 6 weeks, 10 weeks and for live birth.
The p-values for these endpoints of 0.095, 0.035 and 0.025 respectively, provide evidence of an increase in pregnancy percentages with increasing dose level for these endpoints, an effect that became more statistically significant with longer pregnancy duration.
[21] - Treatment difference (Fischer exact test p-value)
OBE001 100mg vs placebo p=0.298
OBE001 300mg vs pllacebo p=0.114
OBE001 900mg vs placebo p=0.064

Post-hoc: Post hoc Live birth (FAS excluding subjects in top quartile of pre-dose P4)

End point title	Post hoc Live birth (FAS excluding subjects in top quartile of pre-dose P4)

End point description:

End point type	Post-hoc

End point timeframe:

women with a live birth at end of pregnancy

End point values	post hoc placebo excl sbjcts in top Q of pre-dose P4	post hoc OBE001 100mg excl sbjcts in top Q of pre-dose P4	post hoc OBE001 300mg excl sbjcts in top Q of pre-dose P4	post hoc OBE001 900mg excl sbjcts in top Q of pre-dose P4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	49	50	35	49
Units: Number of women	15	19	17	25

Statistical analyses

Statistical analysis title	Post hoc live birth (FAS) excl sbj in top Q P4

Statistical analysis description:

Live birth at end of pregnancy full analysis set excluding subjects in top quartile of pre-dose P4

Comparison groups	post hoc placebo excl sbjcts in top Q of pre-dose P4 v post hoc OBE001 100mg excl sbjcts in top Q of pre-dose P4 v post hoc OBE001 300mg excl sbjcts in top Q of pre-dose P4 v post hoc OBE001 900mg excl sbjcts in top Q of pre-dose P4
Number of subjects included in analysis	183
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.025 [22]
Method	Cochran-Armitage trend test

Notes:

[22] - Treatment difference (Fischer exact test p-value)
OBE001 100mg vs placebo p=0.527
OBE001 300mg vs pllacebo p=0.114
OBE001 900mg vs placebo p=0.064

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were collected on an ongoing basis from the day of signed informed consent

Adverse event reporting additional description:

Adverse Event data were collected continuously during the study. Adverse Event data were obtained at scheduled study visits based on the physical examination, vital signs and biological laboratory assessments. In addition, subjects reported AEs spontaneously and/or through questioning.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	placebo

Reporting group description:

The Safety Set consists of all randomised subjects who received placebo to match study medication (analysed according to treatment received)

Reporting group title	100mg OBE001

Reporting group description:

The Safety Set consists of all randomised subjects who received 100mg OBE001 study medication (analysed according to treatment received)

Reporting group title	300mg OBE001

Reporting group description:

The Safety Set consists of all randomised subjects who received 300mg OBE001 study medication (analysed according to treatment received)

Reporting group title	900mg OBE001

Reporting group description:

The Safety Set consists of all randomised subjects who received 900mg OBE001 study medication (analysed according to treatment received)

Reporting group title	placebo - maternal AWFU set (Pregnancy outcome)

Reporting group description:

Included all pregnant women who received placebo and took part in the study follow-up.
Includes adverse events during the course of pregnancy up to and including the end of pregnancy/delivery as well as serious adverse events occurring up to 28 days after delivery.
This was the analysis set for the Pregnancy Outcome data.

Reporting group title	100mg - maternal AWFU set (Pregnancy outcome)

Reporting group description:

Included all pregnant women who received 100mg OBE001 and took part in the study follow-up.
Includes adverse events during the course of pregnancy up to and including the end of pregnancy/delivery as well as serious adverse events occurring up to 28 days after delivery.
This was the analysis set for the Pregnancy Outcome data.

Reporting group title	300mg - maternal AWFU set (Pregnancy Outcome)

Reporting group description:

Included all pregnant women who received 300mg OBE001 and took part in the study follow-up.
Includes adverse events during the course of pregnancy up to and including the end of pregnancy/delivery as well as serious adverse events occurring up to 28 days after delivery.
This was the analysis set for the Pregnancy Outcome data.

Reporting group title	900mg - maternal AWFU set (Pregnancy Outcome)

Reporting group description:

Included all pregnant women who received 900mg OBE001 and took part in the study follow-up.
Includes adverse events during the course of pregnancy up to and including the end of pregnancy/delivery as well as serious adverse events occurring up to 28 days after delivery.
This was the analysis set for the Pregnancy Outcome data.

Reporting group title	placebo - All Infant set (Neonatal)

Reporting group description:

the condition of the new-born at birth and during at least 28 days post-delivery (All Infants (AI) Set) from 23 mothers that received placebo.
This was the analysis set for the Neonatal Health data

Reporting group title	100mg - All infant set (Neonatal)

Reporting group description:

the condition of the new-born at birth and during at least 28 days post-delivery (All Infants (AI) Set), from 29 mothers who received 100mg OBE001.
This was the analysis set for the Neonatal Health data

Reporting group title	300mg - All infant Set (Neonatal)

Reporting group description:

the condition of the new-born at birth and during at least 28 days post-delivery (All Infants (AI) Set), from 25 mothers that received 300mg OBE001
This was the analysis set for the Neonatal Health data

Reporting group title	900mg - All infant set (Neonatal)

Reporting group description:

the condition of the new-born at birth and during at least 28 days post-delivery (All Infants (AI) Set), from 32 mothers that received 900mg OBE001.
This was the analysis set for the Neonatal Health data

Serious adverse events	placebo	100mg OBE001	300mg OBE001
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 65 (3.08%)	2 / 62 (3.23%)	0 / 60 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Congenital, familial and genetic disorders			
Polydactyly			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
Prader-Willi syndrome			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
Talipes			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
Hypoplastic left heart syndrome	Additional description: an SAE for a foetus that was not delivered		

subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
Turner's syndrome	Additional description: An SAE for a foetus that was not delivered		
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
Congenital absence of cranial vault	Additional description: An SAE for a foetus that was not delivered		
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
Caesarean section			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	1 / 65 (1.54%)	1 / 62 (1.61%)	0 / 60 (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
Foetal growth restriction			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
Abortion spontaneous			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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

Haemorrhage in pregnancy			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
Premature labour			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
Premature rupture of membranes			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
Preterm premature rupture of membranes			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
General disorders and administration site conditions			
Death neonatal			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
Reproductive system and breast disorders			
Adnexal torsion			
subjects affected / exposed	1 / 65 (1.54%)	0 / 62 (0.00%)	0 / 60 (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
Ovarian hyperstimulation syndrome			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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
Vaginal haemorrhage			

subjects affected / exposed	0 / 65 (0.00%)	1 / 62 (1.61%)	0 / 60 (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			
Hydronephrosis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (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

Serious adverse events	900mg OBE001	placebo - maternal AWFU set (Pregnancy outcome)	100mg - maternal AWFU set (Pregnancy outcome)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 60 (3.33%)	0 / 19 (0.00%)	2 / 27 (7.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Congenital, familial and genetic disorders			
Polydactyly			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
Prader-Willi syndrome			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
Talipes			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
Hypoplastic left heart syndrome	Additional description: an SAE for a foetus that was not delivered		
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
Turner's syndrome	Additional description: An SAE for a foetus that was not delivered		

subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
Congenital absence of cranial vault	Additional description: An SAE for a foetus that was not delivered		
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	2 / 27 (7.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Caesarean section			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	1 / 60 (1.67%)	0 / 19 (0.00%)	0 / 27 (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 growth restriction			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
Abortion spontaneous			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
Haemorrhage in pregnancy			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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

Premature labour			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
Premature rupture of membranes			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
Preterm premature rupture of membranes			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
General disorders and administration site conditions			
Death neonatal			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
Reproductive system and breast disorders			
Adnexal torsion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
Ovarian hyperstimulation syndrome			
subjects affected / exposed	1 / 60 (1.67%)	0 / 19 (0.00%)	0 / 27 (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
Vaginal haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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
Renal and urinary disorders			
Hydronephrosis			

subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (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

Serious adverse events	300mg - maternal AWFU set (Pregnancy Outcome)	900mg - maternal AWFU set (Pregnancy Outcome)	placebo - All Infant set (Neonatal)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 21 (14.29%)	1 / 27 (3.70%)	2 / 23 (8.70%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Congenital, familial and genetic disorders			
Polydactyly			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (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
Prader-Willi syndrome			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (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
Talipes			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoplastic left heart syndrome	Additional description: an SAE for a foetus that was not delivered		
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (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
Turner's syndrome	Additional description: An SAE for a foetus that was not delivered		
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (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
Congenital absence of cranial vault	Additional description: An SAE for a foetus that was not delivered		

subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (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
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (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
Caesarean section			
subjects affected / exposed	1 / 21 (4.76%)	0 / 27 (0.00%)	0 / 23 (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			
Ectopic pregnancy			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (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
Foetal growth restriction			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (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
Abortion spontaneous			
subjects affected / exposed	0 / 21 (0.00%)	1 / 27 (3.70%)	0 / 23 (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
Haemorrhage in pregnancy			
subjects affected / exposed	1 / 21 (4.76%)	0 / 27 (0.00%)	0 / 23 (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
Premature labour			
subjects affected / exposed	1 / 21 (4.76%)	0 / 27 (0.00%)	0 / 23 (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

Premature rupture of membranes			
subjects affected / exposed	1 / 21 (4.76%)	0 / 27 (0.00%)	0 / 23 (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
Preterm premature rupture of membranes			
subjects affected / exposed	1 / 21 (4.76%)	0 / 27 (0.00%)	0 / 23 (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
General disorders and administration site conditions			
Death neonatal			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (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
Reproductive system and breast disorders			
Adnexal torsion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (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
Ovarian hyperstimulation syndrome			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (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
Vaginal haemorrhage			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (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
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	100mg - All infant set (Neonatal)	300mg - All infant Set (Neonatal)	900mg - All infant set (Neonatal)
Total subjects affected by serious			

adverse events			
subjects affected / exposed	4 / 29 (13.79%)	3 / 25 (12.00%)	1 / 32 (3.13%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Congenital, familial and genetic disorders			
Polydactyly			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prader-Willi syndrome			
subjects affected / exposed	1 / 29 (3.45%)	0 / 25 (0.00%)	0 / 32 (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
Talipes			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (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
Hypoplastic left heart syndrome	Additional description: an SAE for a foetus that was not delivered		
subjects affected / exposed	1 / 29 (3.45%)	0 / 25 (0.00%)	0 / 32 (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
Turner's syndrome	Additional description: An SAE for a foetus that was not delivered		
subjects affected / exposed	1 / 29 (3.45%)	0 / 25 (0.00%)	0 / 32 (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
Congenital absence of cranial vault	Additional description: An SAE for a foetus that was not delivered		
subjects affected / exposed	1 / 29 (3.45%)	0 / 25 (0.00%)	0 / 32 (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
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (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
Caesarean section			

subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (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
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (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
Foetal growth restriction			
subjects affected / exposed	0 / 29 (0.00%)	2 / 25 (8.00%)	0 / 32 (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
Abortion spontaneous			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (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
Haemorrhage in pregnancy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (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
Premature labour			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (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
Premature rupture of membranes			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (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
Preterm premature rupture of membranes			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (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
General disorders and administration			

site conditions			
Death neonatal			
subjects affected / exposed	0 / 29 (0.00%)	1 / 25 (4.00%)	0 / 32 (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			
Adnexal torsion			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (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
Ovarian hyperstimulation syndrome			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (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
Vaginal haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (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
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (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

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	placebo	100mg OBE001	300mg OBE001
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 65 (38.46%)	21 / 62 (33.87%)	22 / 60 (36.67%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			

Caesarean section			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Abortion induced			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Pregnancy, puerperium and perinatal conditions			
Abortion missed			
subjects affected / exposed	2 / 65 (3.08%)	3 / 62 (4.84%)	2 / 60 (3.33%)
occurrences (all)	2	3	2
Abortion spontaneous			
subjects affected / exposed	8 / 65 (12.31%)	2 / 62 (3.23%)	5 / 60 (8.33%)
occurrences (all)	8	2	5
Biochemical pregnancy			
subjects affected / exposed	3 / 65 (4.62%)	0 / 62 (0.00%)	1 / 60 (1.67%)
occurrences (all)	3	0	1
Premature baby			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Foetal growth restriction			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Oligohydramnios			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Small for dates baby			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Gestational diabetes			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Premature labour			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Placenta praevia			

subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Pre-eclampsia			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Threatened labour			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Abortion threatened			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Cervical incompetence			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Gestational hypertension			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Multiple pregnancy			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Premature delivery			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Umbilical cord abnormality			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Uterine contractions abnormal			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 65 (1.54%)	1 / 62 (1.61%)	0 / 60 (0.00%)
occurrences (all)	1	1	2
Reproductive system and breast disorders			

Breast pain			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	2 / 60 (3.33%)
occurrences (all)	0	0	2
Ovarian hyperstimulation syndrome			
subjects affected / exposed	0 / 65 (0.00%)	2 / 62 (3.23%)	3 / 60 (5.00%)
occurrences (all)	0	2	5
Uterine pain			
subjects affected / exposed	1 / 65 (1.54%)	0 / 62 (0.00%)	2 / 60 (3.33%)
occurrences (all)	1	0	2
Vaginal haemorrhage			
subjects affected / exposed	8 / 65 (12.31%)	2 / 62 (3.23%)	2 / 60 (3.33%)
occurrences (all)	12	2	2
Uterine atony			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Neonatal respiratory distress syndrome			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Respiratory failure			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Neonatal asphyxia			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood alkaline phosphatase decreased			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Protein total abnormal			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Streptococcus test positive			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0

Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Cerebrovascular arteriovenous malformation			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 65 (3.08%)	0 / 62 (0.00%)	1 / 60 (1.67%)
occurrences (all)	2	0	1
Headache			
subjects affected / exposed	2 / 65 (3.08%)	3 / 62 (4.84%)	1 / 60 (1.67%)
occurrences (all)	2	3	1
Intraventricular haemorrhage			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Cerebral haemorrhage			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia neonatal			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 65 (4.62%)	3 / 62 (4.84%)	1 / 60 (1.67%)
occurrences (all)	5	3	1
Nausea			
subjects affected / exposed	2 / 65 (3.08%)	0 / 62 (0.00%)	1 / 60 (1.67%)
occurrences (all)	2	0	1
Umbilical hernia			

subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Cholestasis of pregnancy			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Thyroid disorder			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 65 (3.08%)	1 / 62 (1.61%)	0 / 60 (0.00%)
occurrences (all)	2	1	0
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 65 (1.54%)	2 / 62 (3.23%)	0 / 60 (0.00%)
occurrences (all)	1	2	0
Amniotic cavity infection			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Pneumonia			

subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypervitaminosis D			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	900mg OBE001	placebo - maternal AWFU set (Pregnancy outcome)	100mg - maternal AWFU set (Pregnancy outcome)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 60 (25.00%)	7 / 19 (36.84%)	8 / 27 (29.63%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 60 (0.00%)	2 / 19 (10.53%)	1 / 27 (3.70%)
occurrences (all)	0	2	1
Surgical and medical procedures			
Caesarean section			
subjects affected / exposed	0 / 60 (0.00%)	1 / 19 (5.26%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Abortion induced			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1

Pregnancy, puerperium and perinatal conditions			
Abortion missed			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Abortion spontaneous			
subjects affected / exposed	3 / 60 (5.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	3	0	0
Biochemical pregnancy			
subjects affected / exposed	2 / 60 (3.33%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Premature baby			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Foetal growth restriction			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Oligohydramnios			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Small for dates baby			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gestational diabetes			
subjects affected / exposed	0 / 60 (0.00%)	1 / 19 (5.26%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Premature labour			
subjects affected / exposed	0 / 60 (0.00%)	1 / 19 (5.26%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Placenta praevia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 19 (5.26%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Pre-eclampsia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Threatened labour			

subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Abortion threatened			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Cervical incompetence			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gestational hypertension			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Multiple pregnancy			
subjects affected / exposed	0 / 60 (0.00%)	1 / 19 (5.26%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Premature delivery			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Umbilical cord abnormality			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Uterine contractions abnormal			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 60 (3.33%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Ovarian hyperstimulation syndrome			
subjects affected / exposed	2 / 60 (3.33%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Uterine pain			

subjects affected / exposed	2 / 60 (3.33%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Vaginal haemorrhage			
subjects affected / exposed	3 / 60 (5.00%)	2 / 19 (10.53%)	1 / 27 (3.70%)
occurrences (all)	4	2	1
Uterine atony			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Neonatal respiratory distress syndrome			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Respiratory failure			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Neonatal asphyxia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood alkaline phosphatase decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Protein total abnormal			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Streptococcus test positive			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Cerebrovascular arteriovenous malformation			

subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	3 / 60 (5.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	3	0	0
Intraventricular haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Cerebral haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia neonatal			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 60 (1.67%)	1 / 19 (5.26%)	1 / 27 (3.70%)
occurrences (all)	1	1	1
Umbilical hernia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			

Cholestasis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Cholestasis of pregnancy			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 19 (5.26%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 60 (0.00%)	2 / 19 (10.53%)	1 / 27 (3.70%)
occurrences (all)	0	2	1
Thyroid disorder			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 19 (5.26%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Amniotic cavity infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Nasopharyngitis			

subjects affected / exposed	0 / 60 (0.00%)	1 / 19 (5.26%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Viral infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypervitaminosis D			
subjects affected / exposed	0 / 60 (0.00%)	0 / 19 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 60 (0.00%)	1 / 19 (5.26%)	0 / 27 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	300mg - maternal AWFU set (Pregnancy Outcome)	900mg - maternal AWFU set (Pregnancy Outcome)	placebo - All Infant set (Neonatal)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 21 (38.10%)	12 / 27 (44.44%)	1 / 23 (4.35%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 21 (9.52%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Surgical and medical procedures			
Caesarean section			
subjects affected / exposed	1 / 21 (4.76%)	2 / 27 (7.41%)	0 / 23 (0.00%)
occurrences (all)	1	2	0
Abortion induced			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Pregnancy, puerperium and perinatal conditions			
Abortion missed			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Abortion spontaneous			

subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Biochemical pregnancy			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Premature baby			
subjects affected / exposed	0 / 21 (0.00%)	1 / 27 (3.70%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Foetal growth restriction			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Oligohydramnios			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Small for dates baby			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Gestational diabetes			
subjects affected / exposed	1 / 21 (4.76%)	1 / 27 (3.70%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Premature labour			
subjects affected / exposed	1 / 21 (4.76%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Placenta praevia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 27 (3.70%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Pre-eclampsia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Threatened labour			
subjects affected / exposed	1 / 21 (4.76%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Abortion threatened			
subjects affected / exposed	0 / 21 (0.00%)	1 / 27 (3.70%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Cervical incompetence			

subjects affected / exposed	0 / 21 (0.00%)	1 / 27 (3.70%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Gestational hypertension			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Multiple pregnancy			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Premature delivery			
subjects affected / exposed	1 / 21 (4.76%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Umbilical cord abnormality			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Uterine contractions abnormal			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Ovarian hyperstimulation syndrome			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Uterine pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 21 (0.00%)	1 / 27 (3.70%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Uterine atony			

subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Neonatal respiratory distress syndrome			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Respiratory failure			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Neonatal asphyxia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood alkaline phosphatase decreased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 27 (3.70%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Protein total abnormal			
subjects affected / exposed	1 / 21 (4.76%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Streptococcus test positive			
subjects affected / exposed	0 / 21 (0.00%)	1 / 27 (3.70%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Cerebrovascular arteriovenous malformation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Headache			

subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Intraventricular haemorrhage			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Cerebral haemorrhage			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia neonatal			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	1 / 21 (4.76%)	1 / 27 (3.70%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Umbilical hernia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 21 (4.76%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Cholestasis of pregnancy			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Dermatitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 21 (0.00%)	2 / 27 (7.41%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Thyroid disorder			
subjects affected / exposed	0 / 21 (0.00%)	1 / 27 (3.70%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Amniotic cavity infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 21 (4.76%)	1 / 27 (3.70%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 21 (0.00%)	1 / 27 (3.70%)	0 / 23 (0.00%)
occurrences (all)	0	1	0

Metabolism and nutrition disorders			
Hypervitaminosis D			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 21 (0.00%)	0 / 27 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	100mg - All infant set (Neonatal)	300mg - All infant Set (Neonatal)	900mg - All infant set (Neonatal)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 29 (17.24%)	3 / 25 (12.00%)	2 / 32 (6.25%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Caesarean section			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Abortion induced			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Pregnancy, puerperium and perinatal conditions			
Abortion missed			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Abortion spontaneous			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Biochemical pregnancy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Premature baby			
subjects affected / exposed	3 / 29 (10.34%)	1 / 25 (4.00%)	2 / 32 (6.25%)
occurrences (all)	3	1	2
Foetal growth restriction			

subjects affected / exposed	1 / 29 (3.45%)	1 / 25 (4.00%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
Oligohydramnios			
subjects affected / exposed	0 / 29 (0.00%)	1 / 25 (4.00%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Small for dates baby			
subjects affected / exposed	1 / 29 (3.45%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Gestational diabetes			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Premature labour			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Placenta praevia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Pre-eclampsia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Threatened labour			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Abortion threatened			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Cervical incompetence			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Gestational hypertension			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Multiple pregnancy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Premature delivery			

subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Umbilical cord abnormality			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Uterine contractions abnormal			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Ovarian hyperstimulation syndrome			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Uterine pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Uterine atony			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Neonatal respiratory distress syndrome			
subjects affected / exposed	4 / 29 (13.79%)	0 / 25 (0.00%)	2 / 32 (6.25%)
occurrences (all)	4	0	2
Respiratory failure			

subjects affected / exposed	1 / 29 (3.45%)	0 / 25 (0.00%)	2 / 32 (6.25%)
occurrences (all)	1	0	2
Neonatal asphyxia			
subjects affected / exposed	1 / 29 (3.45%)	1 / 25 (4.00%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
Investigations			
Blood alkaline phosphatase decreased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Protein total abnormal			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Streptococcus test positive			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	2 / 29 (6.90%)	0 / 25 (0.00%)	2 / 32 (6.25%)
occurrences (all)	2	0	2
Cerebrovascular arteriovenous malformation			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Intraventricular haemorrhage			
subjects affected / exposed	1 / 29 (3.45%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Cerebral haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0

Blood and lymphatic system disorders			
Anaemia neonatal			
subjects affected / exposed	1 / 29 (3.45%)	0 / 25 (0.00%)	2 / 32 (6.25%)
occurrences (all)	1	0	2
Anaemia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Umbilical hernia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Abdominal pain upper			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Cholestasis of pregnancy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Thyroid disorder			

subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Amniotic cavity infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 25 (0.00%)	2 / 32 (6.25%)
occurrences (all)	1	0	2
Pneumonia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypervitaminosis D			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Iron deficiency			
subjects affected / exposed	0 / 29 (0.00%)	0 / 25 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 August 2014	Protocol amendment No. 1 (country specific for Denmark) was issued on 21st August 2014 and defined the following changes: - Inclusion criteria changed to allow the use of vaginal micronized progesterone tablets at 300 mg per day (3 x 100 mg) according to the approved product label for Lutinus/Endometrin 100 mg vaginal tablets.
04 September 2014	Protocol amendment No. 2 (country specific for the United Kingdom) was issued on 4th September 2014 and defined the following changes: - Emergency un-blinding procedures were updated.
10 October 2014	Protocol amendment No. 3 (all countries except Denmark) was issued on 10th October 2014 and defined the following changes. - Clinical pregnancy rate to be measured at 6 weeks post ET instead of 5 weeks post OPU day; - Progesterone for luteal support to be started in the evening of the OPU day or the morning of the day after OPU; - Addition of an analysis of the relationship between decrease in uterine contractions and pregnancy rates; - Embryo transfer to be performed by a skilled and experienced clinician. Where possible it should be the same clinician; - Wording on emergency un-blinding clarified; - Number of sites increased from 20 to 30.
24 October 2014	Protocol amendment No. 4 (country specific for Denmark including protocol amendments 01, 02, and 03) was issued on 24th October 2015 and defined the following changes: - Wording on emergency un-blinding clarified; - Clinical pregnancy rate to be measured at 6 weeks post ET instead of 5 weeks post OPU day; - Progesterone for luteal support to be started in the evening of the OPU day or the morning of the day after OPU; - Embryo transfer to be performed by a skilled and experienced clinician. Where possible it should be the same clinician; - Addition of an analysis of the relationship between decrease in uterine contractions and pregnancy rates; - Number of sites increased from 20 to 30.
20 March 2015	Protocol amendment No 5 (General) was issued on 20th March 2015 and defined the following changes: - Addition of a 6-month infant safety follow-up using the ASQ-3; - Addition of a sensitivity analysis according to the difficulty of embryo transfer; - Clarification of procedure for premature discontinuation of the study for safety reasons; - Consistent use of the term “subject” instead of patient; - Amended timing of baseline assessments to allow for time constraints at sites.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported