Clinical trial results:
A phase 2, double-blind, parallel group, randomised, placebo controlled, proof of concept study to assess the safety and efficacy of OBE001 after oral administration in pregnant women with threatened preterm labour.

Summary

EudraCT number	2014-003217-28
Trial protocol	ES DE BE PL GB CZ
Global end of trial date	28 October 2016

Results information

Result version number	v1 (current)
This version publication date	12 November 2017
First version publication date	12 November 2017

Trial information

Trial identification

Sponsor protocol code	14-OBE001-016

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, Switzerland, 1228
Public contact	Clinical Trials Information, ObsEva SA, 41 0225523840, clinicaltrials@obseva.ch
Scientific contact	Clinical Trials Information, ObsEva SA, 41 0225523840, 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	24 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 October 2016
Global end of trial reached?	Yes
Global end of trial date	28 October 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of OBE001 with placebo to delay preterm birth by 7 days.

Protection of trial subjects:

This study was performed in accordance with the protocol, the Declaration of Helsinki, the ICH Harmonised Tripartite Guideline for GCP, and all applicable local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 January 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Switzerland: 2
Worldwide total number of subjects	10
EEA total number of subjects	8

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)	10
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Date of first subject first visit 11 Jun 2015
Date of last subject last visit 24 Aug 2016
A total of 25 sites were opened, 3 in Belgium, 4 in Switzerland, 4 in Germany, 5 in Spain, 3 in the UK, and 6 in Poland. Of these only 6 sites recruited subjects.

Pre-assignment

Screening details:

To be included in this study, women had to present with preterm labour with a high risk to progress to a birth within 7 days i.e. ≥ 3 contractions per 30 mins plus one other sign of the progression of labour such as a positive foetal fibronectin test, a cervical length less than 25 mm or cervical dilatation 2–4 cm.

Period 1

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

Blinding implementation details:

Prior to the start of the study, the randomisation list was generated by the designated statistician and transmitted to the assigned clinical packaging organisation for labelling and to a fully web-integrated IWRS.

Arms

Are arms mutually exclusive?	Yes
Arm title	OBE001

Arm description:

OBE001 oral dispersible tablets for 7 days with a loading dose of 200 mg on Day 1 followed by 100 mg/day for 6 days.

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

Dosage and administration details:

Each subject was assigned a treatment kit containing 3 aluminium-aluminium blisters as follows:
Day 1: 4 cavities/blister (1 x 200 mg dose)
Day 2-4: 6 cavities/blister (3 x 100 mg doses)
Day 5-7: 6 cavities/blister (3 x 100 mg doses)

Arm title	placebo

Arm description:

matching placebo - oral dispersible tablets for 7 days with a loading dose of 200 mg on Day 1 followed by 100 mg/day for 6 days.

Arm type	Placebo
Investigational medicinal product name	placebo (to match OBE001)
Investigational medicinal product code	placebo
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Each subject was assigned a treatment kit containing 3 aluminium-aluminium blisters as follows:
Day 1: 4 cavities/blister (1 x 200 mg dose)
Day 2-4: 6 cavities/blister (3 x 100 mg doses)
Day 5-7: 6 cavities/blister (3 x 100 mg doses)

Number of subjects in period 1	OBE001	placebo
Started	4	6
Completed	4	3
Not completed	0	3
didn't want to visit site except newborn follow-up	-	1
went into labour and did not start IMP treatment	-	1
Lost to follow-up	-	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	10	10	
Age categorical Units: Subjects			
Age continuous			
FAS			
Units: years arithmetic mean full range (min-max)	 29.9 19 to 37	 -	
Gender categorical Units: Subjects			
Female	10	10	

Subject analysis sets

Subject analysis set title	Full Analysis Set - OBE001
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS included all subjects randomized who received at least one dose of OBE001

Subject analysis set title	Full Analysis Set - Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS included all subjects randomized who received at least one dose of placebo

Reporting group values	Full Analysis Set - OBE001	Full Analysis Set - Placebo	
Number of subjects	4	5	
Age categorical Units: Subjects			
Age continuous			
FAS			
Units: years arithmetic mean full range (min-max)	 28 20 to 33	 30 19 to 35	
Gender categorical Units: Subjects			
Female	4	5	

End points

End points reporting groups

Reporting group title	OBE001
Reporting group description:	
OBE001 oral dispersible tablets for 7 days with a loading dose of 200 mg on Day 1 followed by 100 mg/day for 6 days.	
Reporting group title	placebo
Reporting group description:	
matching placebo - oral dispersible tablets for 7 days with a loading dose of 200 mg on Day 1 followed by 100 mg/day for 6 days.	
Subject analysis set title	Full Analysis Set - OBE001
Subject analysis set type	Full analysis
Subject analysis set description:	
The FAS included all subjects randomized who received at least one dose of OBE001	
Subject analysis set title	Full Analysis Set - Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
The FAS included all subjects randomized who received at least one dose of placebo	

Primary: incidence of women delivering within 7 days post first dose

End point title	incidence of women delivering within 7 days post first dose
End point description:	
End point type	Primary
End point timeframe:	
The primary endpoint was the incidence of women delivering within 7 days post first dose (i.e. within 168 hours of first dose).	

End point values	OBE001	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: number of women	1	1		

Statistical analyses

Statistical analysis title	statistical analysis plan dated 19 October 2016
Statistical analysis description:	
All statistical analyses and data processing were performed using SAS® Version 9.4 on a Windows 7 operating system. Descriptive statistics are provided for all variables in the summary tables by treatment group according to the type of variable summarized. Quantitative variables are summarised using number (n), arithmetic mean, standard deviation (SD), median, 1st and 3rd quartiles, minimum and maximum. Categorical variables are summarised using count and percentages.	
Comparison groups	OBE001 v placebo

Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 1
Method	Fisher exact

Notes:

[1] - Analyses were performed on the FAS set only.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Data on AEs was obtained at scheduled and unscheduled study visits, based on information spontaneously provided by the subject and/ or through questioning of the subject.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	OBE001 Maternal TEAEs

Reporting group description:

An AE was classified as a TEAE if it started on or after the date of randomised study medication intake (AE onset date ≥ first date of randomised study medication intake) and up to 7 days after treatment end (AE onset date ≤ last date of randomised study medication intake +7 days).

Reporting group title	placebo Maternal TEAEs

Reporting group description:

An AE was classified as a TEAE if it started on or after the date of randomised study medication intake (AE onset date ≥ first date of randomised study medication intake) and up to 7 days after treatment end (AE onset date ≤ last date of randomised study medication intake +7 days).

Reporting group title	OBE001 Maternal Post-TEAEs

Reporting group description:

An AE was classed as a post-treatment AE if it started after 7 days after treatment end (AE onset date > last date of randomised study medication intake +7 days).

Reporting group title	placebo Maternal Post-TEAEs

Reporting group description:

An AE was classed as a post-treatment AE if it started after 7 days after treatment end (AE onset date > last date of randomised study medication intake +7 days).

Reporting group title	OBE001 Foetal TEAEs

Reporting group description:

All foetal TEAEs, defined as adverse events with onset date ≥ date of randomized study medication intake are provided here

Reporting group title	placebo Foetal TEAEs

Reporting group description:

All foetal TEAEs, defined as adverse events with onset date ≥ date of randomized study medication intake are presented here

Reporting group title	OBE001 Infant TEAEs

Reporting group description:

Infant AEs were defined as any AE detected in an infant, observed between the day of delivery and the last visit. Infant adverse events are presented in the same way as maternal adverse events with the exception of pre-treatment and post-treatment adverse events (as these are not applicable for infants).

Reporting group title	placebo Infant TEAEs

Reporting group description:

Infant AEs were defined as any AE detected in an infant, observed between the day of delivery and the last visit. Infant adverse events are presented in the same way as maternal adverse events with the exception of pre-treatment and post-treatment adverse events (as these are not applicable for infants).

Serious adverse events	OBE001 Maternal TEAEs	placebo Maternal TEAEs	OBE001 Maternal Post-TEAEs
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Pregnancy, puerperium and perinatal conditions			
Foetal distress syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (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	placebo Maternal Post-TEAEs	OBE001 Foetal TEAEs	placebo Foetal TEAEs
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Pregnancy, puerperium and perinatal conditions			
Foetal distress syndrome			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 5 (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
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OBE001 Infant TEAEs	placebo Infant TEAEs	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
number of deaths (all causes)	0	0	

number of deaths resulting from adverse events	0	0	
Pregnancy, puerperium and perinatal conditions			
Foetal distress syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	OBE001 Maternal TEAEs	placebo Maternal TEAEs	OBE001 Maternal Post-TEAEs
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	4 / 5 (80.00%)	2 / 4 (50.00%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Phototherapy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pregnancy, puerperium and perinatal			

conditions			
Postpartum haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Foetal distress syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia of pregnancy acute			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Small intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Vaginal discharge			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
apnoea neonatal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neonatal respiratory distress syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Swelling face			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Spinal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Mastitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	placebo Maternal Post-TEAEs	OBE001 Foetal TEAEs	placebo Foetal TEAEs
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Phototherapy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pregnancy, puerperium and perinatal conditions			
Postpartum haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Foetal distress syndrome			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia of pregnancy acute			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Nausea			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Small intestinal obstruction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vaginal discharge			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
apnoea neonatal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neonatal respiratory distress syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Swelling face			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Spinal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Mastitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	OBE001 Infant TEAEs	placebo Infant TEAEs	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	3 / 5 (60.00%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Surgical and medical procedures			
Phototherapy			
subjects affected / exposed	0 / 4 (0.00%)	2 / 5 (40.00%)	
occurrences (all)	0	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Pregnancy, puerperium and perinatal conditions			

Postpartum haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Foetal distress syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia of pregnancy acute			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Small intestinal obstruction			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Vaginal discharge			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
apnoea neonatal			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Neonatal respiratory distress syndrome			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 4 (0.00%)	3 / 5 (60.00%)	
occurrences (all)	0	3	
Skin and subcutaneous tissue disorders			
Swelling face			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Spinal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Mastitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 December 2014	The study rationale was clarified and expanded including: · The 2 year observational, safety follow-up study was included as an extension to the current study instead of existing as a stand-alone protocol. · Clarification of the definition of "end of study".
07 September 2015	· Amendments to the wash-out period for excluded medication. · Further clarification of exclusion criterion #3d. · Clarification of the SAE reporting timescale
07 December 2015	· Additional assessment of uterine contractions at 3 hours in order to assess treatment efficacy at peak drug concentrations. · Modification of overly restrictive definition of preterm labour to help increase recruitment rates. · Exclusion criterion of "eclampsia or severe pre-eclampsia" modified to "eclampsia or pre-eclampsia". · Modification of ECG requirements on entry and additional exclusion of subjects for whom treatment with parenteral magnesium sulphate was anticipated. · Further modification of the specified washout periods for certain tocolytics based on their pharmacokinetic properties. · Modified definition of preterm labour. · Addition of safety information from recently updated investigators brochure. · Additional increase in the number of centres.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
13 July 2016	The study aimed to recruit 100 subjects by the end of 2015. Due to difficulties with recruitment the sponsor decided to terminate the study on 13 July 2016. Investigators were notified on the same day and asked not to recruit any more subjects after 25 July 2016. Only 10 subjects were randomised into the study.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Many of the statistical analyses described in the study protocol were not performed due to the Sponsor's decision to terminate the study early. The statistical analyses performed are primarily only summaries, plus listings of the data.

Notes: