



## Clinical trial results:

### Randomized, Double-blind, Multicenter, Phase III Study Comparing the Efficacy and Safety of Retosiban Versus Atosiban Therapy for Women in Spontaneous Preterm Labor

#### Summary

EudraCT number	2014-001826-13
Trial protocol	BE GB SE ES DE IT FR
Global end of trial date	25 August 2017

#### Results information

Result version number	v3
This version publication date	31 August 2018
First version publication date	10 March 2018
Version creation reason	

#### Trial information

##### Trial identification

Sponsor protocol code	200721
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001359-PIP01-12
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	13 December 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 August 2017
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate the superiority of retosiban to prolong pregnancy compared with atosiban

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 March 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	Belgium: 6
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Israel: 35
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Mexico: 24
Country: Number of subjects enrolled	Korea, Republic of: 13
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	United Kingdom: 1
Worldwide total number of subjects	97
EEA total number of subjects	25

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)	3
Adults (18-64 years)	94
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

ZINN was a randomized, double-blind, double-dummy multicenter study to compare efficacy and safety of retosiban versus atosiban in female participants aged 12 to 45 years with an uncomplicated singleton pregnancy in preterm labor with intact membranes between 24 0/7 and 33 6/7 weeks gestation.

### Pre-assignment

Screening details:

From 330 planned participants 100 were enrolled and 97 were randomized to receive either retosiban or atosiban intravenous (IV) infusion in a ratio of 1:1. Two participants randomized to retosiban and 1 participant randomized to atosiban did not receive the study treatment as they were not eligible. The study was terminated early due to feasibility

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Retosiban

Arm description:

Participants were administered 6 milligram (mg) IV loading dose of retosiban over 5 minutes followed by a 6 milligram per hour (mg/hour) continuous infusion of retosiban over 48 hours. Participants with an inadequate response any time after first hour of treatment were administered another 6 mg retosiban loading dose followed by 12 mg/hour continuous infusion for remainder of 48-hour treatment period.

Arm type	Experimental
Investigational medicinal product name	Retosiban
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Retosiban was available as a clear, colorless solution for infusion at a concentration of 15 milligrams per milliliter (mg/mL).

<b>Arm title</b>	Atosiban
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Arm description:

Participants were administered atosiban in 3 successive stages. An initial bolus dose of 6.75 mg using atosiban 6.75 mg/0.9 milliliter (mL) solution for injection, followed by continuous high dose infusion at 18 mg/hour for 3 hours, then a lower 6 mg/hour infusion for the remainder of the 48-hour using the atosiban 37.5 mg/5 mL concentrate for solution.

Arm type	Active comparator
Investigational medicinal product name	Atosiban
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atosiban was available as a clear, colorless solution for injection at a concentration of 6.75 mg/0.9 mL and 7.5 mg/mL solution for infusion

<b>Number of subjects in period 1</b>	Retosiban	Atosiban
Started	47	50
Completed	43	48
Not completed	4	2
Consent withdrawn by subject	2	1
Lost to follow-up	2	1

## Baseline characteristics

### Reporting groups

Reporting group title	Retosiban
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Reporting group description:

Participants were administered 6 milligram (mg) IV loading dose of retosiban over 5 minutes followed by a 6 milligram per hour (mg/hour) continuous infusion of retosiban over 48 hours. Participants with an inadequate response any time after first hour of treatment were administered another 6 mg retosiban loading dose followed by 12 mg/hour continuous infusion for remainder of 48-hour treatment period.

Reporting group title	Atosiban
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Reporting group description:

Participants were administered atosiban in 3 successive stages. An initial bolus dose of 6.75 mg using atosiban 6.75 mg/0.9 milliliter (mL) solution for injection, followed by continuous high dose infusion at 18 mg/hour for 3 hours, then a lower 6 mg/hour infusion for the remainder of the 48-hour using the atosiban 37.5 mg/5 mL concentrate for solution.

Reporting group values	Retosiban	Atosiban	Total
Number of subjects	47	50	97
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	27.7 ± 6.15	27.1 ± 5.66	-
Gender categorical Units: Subjects			
Female	47	50	97
Male	0	0	0

## End points

### End points reporting groups

Reporting group title	Retosiban
Reporting group description:	
Participants were administered 6 milligram (mg) IV loading dose of retosiban over 5 minutes followed by a 6 milligram per hour (mg/hour) continuous infusion of retosiban over 48 hours. Participants with an inadequate response any time after first hour of treatment were administered another 6 mg retosiban loading dose followed by 12 mg/hour continuous infusion for remainder of 48-hour treatment period.	
Reporting group title	Atosiban
Reporting group description:	
Participants were administered atosiban in 3 successive stages. An initial bolus dose of 6.75 mg using atosiban 6.75 mg/0.9 milliliter (mL) solution for injection, followed by continuous high dose infusion at 18 mg/hour for 3 hours, then a lower 6 mg/hour infusion for the remainder of the 48-hour using the atosiban 37.5 mg/5 mL concentrate for solution.	
Subject analysis set title	Retosiban
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants were administered 6 milligram (mg) IV loading dose of retosiban over 5 minutes followed by a 6 milligram per hour (mg/hour) continuous infusion of retosiban over 48 hours. Participants with an inadequate response any time after first hour of treatment were administered another 6 mg retosiban loading dose followed by 12 mg/hour continuous infusion for remainder of 48-hour treatment period. Data is a combined data set. Data is presented for 10 participants from retosiban arm of study 200719 (NCT02377466) and 43 participants from retosiban arm of study 200721 (NCT02292771).	

### Primary: Time to delivery from the start of investigational product (IP) administration

End point title	Time to delivery from the start of investigational product (IP) administration
End point description:	
Time to delivery is the number of days from the first dose of study treatment until delivery. The time to delivery was calculated as the days between the delivery and start time of the study treatment infusion using the formula: Time to delivery (days) = (date and time of delivery minus date and time of start of infusion) divided by (24 multiplied by 60). The adjusted mean number of days to delivery along with standard error has been presented. Maternal intent-to-treat (ITT) Population comprised of all mothers randomly assigned to treatment who have been exposed to study treatment irrespective of their compliance to the planned course of treatment.	
End point type	Primary
End point timeframe:	
Up to 17 weeks	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[1]</sup>	50 <sup>[2]</sup>		
Units: Days				
arithmetic mean (standard error)				
Days	32.51 (± 2.990)	33.71 (± 2.531)		

Notes:

[1] - Maternal ITT Population

[2] - Maternal ITT Population

## Statistical analyses

<b>Statistical analysis title</b>	Statistical analysis 1
Comparison groups	Retosiban v Atosiban
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3797
Method	Finite mixture model
Parameter estimate	Mean difference (final values)
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.879
upper limit	6.479

## Secondary: Number of participants with births prior to 37 0/7 Weeks gestation

End point title	Number of participants with births prior to 37 0/7 Weeks gestation
End point description: Gestational age (GA) at birth (weeks) is defined as the GA when the baby is born. Participants were considered to have delivered prior to 37 0/7 weeks, that is preterm , if the GA at birth is less than 37 0/7 weeks. The number of participants who delivered prior to 37 0/7 weeks gestation has been presented. Logistic regression model was used to calculate p-values.	
End point type	Secondary
End point timeframe: Up to 13 weeks	

<b>End point values</b>	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[3]</sup>	50 <sup>[4]</sup>		
Units: Participants				
Participants	25	28		

Notes:

[3] - Maternal ITT Population

[4] - Maternal ITT Population

## Statistical analyses

<b>Statistical analysis title</b>	Statistical analysis 1
Comparison groups	Atosiban v Retosiban



Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.952
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	2.18

## Secondary: Number of participants with births at term

End point title	Number of participants with births at term
End point description:	
Participants were considered to have delivered at term if the gestational age was $\geq 37$ 0/7. The number of participants who delivered at term, that is, 37 0/7 to 41 6/7 weeks gestation has been presented. Logistic regression model was used to calculate p-values.	
End point type	Secondary
End point timeframe:	
Up to 17 weeks	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[5]</sup>	50 <sup>[6]</sup>		
Units: Participants				
Participants	21	22		

Notes:

[5] - Maternal ITT Population

[6] - Maternal ITT Population

## Statistical analyses

<b>Statistical analysis title</b>	Statistical analysis 1
Comparison groups	Atosiban v Retosiban
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.952
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	2.29

## Secondary: Length of neonatal hospital stay

End point title	Length of neonatal hospital stay
End point description:	
The length of stay was collected from medical records and was calculated as the days between the delivery date and time and discharge date and time. Log of length of stay was calculated as treatment plus GA at randomization plus established progesterone use based on Analysis of covariance (ANCOVA) model. The p-value was calculated using t-test method. Neonatal ITT Population comprised of all neonates whose mothers were the randomized participants who have been exposed to study treatment, that is, mothers from the ITT Population.	
End point type	Secondary
End point timeframe:	
Up to 28 days post estimated date of delivery (EDD) of 40 0/7 weeks gestation	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[7]</sup>	50 <sup>[8]</sup>		
Units: Days				
least squares mean (confidence interval 95%)				
Days	4.98 (3.54 to 6.99)	4.38 (3.15 to 6.09)		

Notes:

[7] - Neonatal ITT Population

[8] - Neonatal ITT Population

## Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Retosiban v Atosiban
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5672
Method	ANCOVA
Parameter estimate	Ratio
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.76

Variability estimate	Standard error of the mean
Dispersion value	0.222

## Secondary: Number of neonates with composite neonatal morbidity and mortality

End point title	Number of neonates with composite neonatal morbidity and mortality
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End point description:

The neonatal composite endpoint was determined from review of medical records and included the following components: fetal or neonatal death, Respiratory Distress Syndrome (RDS), bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC) or isolated perforation, sepsis based on positive blood culture with clinical features of sepsis, meningitis based on positive results for cerebrospinal fluid culture performed as part of infection workup, retinopathy of prematurity (ROP), Intraventricular Hemorrhage (IVH), white matter injury and cerebellar hemorrhage.

End point type	Secondary
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End point timeframe:

Up to 28 weeks after EDD (40 weeks gestation)

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[9]</sup>	50 <sup>[10]</sup>		
Units: Participants				
Participants	3	2		

Notes:

[9] - Neonatal ITT Population

[10] - Neonatal ITT Population

## Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Retosiban v Atosiban
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5066
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	11.71

## Secondary: Number of neonates with any composite neonatal morbidity and mortality, excluding RDS

End point title	Number of neonates with any composite neonatal morbidity and mortality, excluding RDS
End point description:	
The neonatal composite endpoint was determined from review of medical records and included the following components: fetal or neonatal death, RDS, BPD, NEC or isolated perforation, sepsis based on positive blood culture with clinical features of sepsis, meningitis based on positive results for cerebrospinal fluid culture performed as part of infection workup, ROP, IVH, white matter injury and cerebellar hemorrhage. Number of neonates with any composite neonatal morbidity and mortality component, excluding RDS has been presented.	
End point type	Secondary
End point timeframe:	
Up to 28 weeks after EDD (40 weeks gestation)	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[11]</sup>	50 <sup>[12]</sup>		
Units: Participants				
Participants	0	1		

Notes:

[11] - Neonatal ITT Population

[12] - Neonatal ITT Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of neonates with each individual component of composite neonatal morbidity and mortality

End point title	Number of neonates with each individual component of composite neonatal morbidity and mortality
End point description:	
The neonatal composite endpoint was determined from review of medical records and included the following components: fetal or neonatal death, RDS, BPD, NEC or isolated perforation, sepsis based on positive blood culture with clinical features of sepsis, meningitis based on positive results for cerebrospinal fluid culture performed as part of infection workup, ROP, IVH, cerebellar hemorrhage and white matter injury included Periventricular Leukomalacia PVL), porencephalic cyst, and persistent ventriculomegaly. Number of neonates with with each individual component of the composite neonatal morbidity and mortality has been presented.	
End point type	Secondary
End point timeframe:	
Up to 28 weeks after EDD (40 weeks gestation)	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[13]</sup>	50 <sup>[14]</sup>		
Units: Participants				
Fetal death	0	0		
Neonatal death	0	1		
RDS	3	1		

BPD	0	0		
NEC or isolated perforation	0	0		
Sepsis	0	0		
Meningitis	0	0		
ROP	0	0		
IVH	0	0		
PVL	0	0		
Porencephalic Cyst	0	0		
Persistent Ventriculomegaly	0	0		
Cerebellar Hemorrhage	0	0		

Notes:

[13] - Neonatal ITT Population

[14] - Neonatal ITT Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Length of stay in specialized care unit

End point title	Length of stay in specialized care unit
End point description:	
Length of neonatal stay in specialized care unit like Intensive Care Unit (ICU) or Neonatal Intensive Care Unit (NICU) are reported.	
End point type	Secondary
End point timeframe:	
Up to 28 days post EDD (40 0/7 weeks gestation)	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[15]</sup>	50 <sup>[16]</sup>		
Units: Days				
median (full range (min-max))				
Days	13.65 (3.5 to 57.5)	12.49 (7.6 to 21.8)		

Notes:

[15] - Neonatal Safety Population

[16] - Neonatal Safety Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of newborn participants with hospital readmission

End point title	Number of newborn participants with hospital readmission
End point description:	
Newborn hospital readmission following hospitalization for birth was obtained from the newborn's medical records. Only those participants with data available at the specified data points were analyzed.	
End point type	Secondary
End point timeframe:	
Up to 28 days of EDD (40 0/7 weeks gestation)	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46 <sup>[17]</sup>	50 <sup>[18]</sup>		
Units: Participants				
Participants	2	3		

Notes:

[17] - Neonatal Safety Population

[18] - Neonatal Safety Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with births prior to 28 0/7 weeks gestation

End point title	Number of participants with births prior to 28 0/7 weeks gestation
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End point description:

The number of participants who delivered prior to 28 0/7 weeks gestation has been presented. Only those maternal participants who were randomized prior to 28 0/7 week's gestation and delivered were included.

End point type	Secondary
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End point timeframe:

Up to 4 weeks

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	50		
Units: Participats				
Participants	0	0		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with births prior to 32 0/7 weeks gestation

End point title	Number of participants with births prior to 32 0/7 weeks gestation
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End point description:

Number of participants who delivered prior to 32 0/7 weeks gestation has been presented. Only those maternal participants who were randomized prior to 32 0/7 week's gestation and delivered were included.

End point type	Secondary
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End point timeframe:

Up to 8 weeks

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[19]</sup>	50 <sup>[20]</sup>		
Units: Participants				
Participants	3	3		

Notes:

[19] - Maternal ITT Population

[20] - Maternal ITT Population

## Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Atosiban v Retosiban
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.779
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	4.84

## Secondary: Number of participants with births prior to 35 0/7 weeks gestation

End point title	Number of participants with births prior to 35 0/7 weeks gestation
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End point description:

Number of participants who delivered prior to 35 0/7 weeks gestation has been presented. Only those maternal participants who were randomized prior to 35 0/7 week's gestation and delivered were included.

End point type	Secondary
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End point timeframe:

Up to 11 weeks

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[21]</sup>	50 <sup>[22]</sup>		
Units: Participants				
Participants	14	14		

Notes:

[21] - Maternal ITT Population

[22] - Maternal ITT Population

### Statistical analyses

<b>Statistical analysis title</b>	Statistical analysis 1
Comparison groups	Retosiban v Atosiban
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6646
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	2.9

### Secondary: Number of participants with births <=7 days from the first study treatment

End point title	Number of participants with births <=7 days from the first study treatment
End point description:	
Number of participants who delivered in less than or equal to 7 days from first dose of study treatment has been presented.	
End point type	Secondary
End point timeframe:	
Up to 7 days	

<b>End point values</b>	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[23]</sup>	50 <sup>[24]</sup>		
Units: Participants				
Participants	10	7		

Notes:

[23] - Maternal ITT Population

[24] - Maternal ITT Population

### Statistical analyses



<b>Statistical analysis title</b>	Statistical analysis 1
Comparison groups	Retosiban v Atosiban
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1432
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	7.24

### Secondary: Number of participants with births <=48 hours from the first study treatment

End point title	Number of participants with births <=48 hours from the first study treatment
End point description: Number of participants who delivered in less than or equal to 48 hours from first dose of study treatment has been presented.	
End point type	Secondary
End point timeframe: Up to 48 hours	

<b>End point values</b>	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[25]</sup>	50 <sup>[26]</sup>		
Units: Participants				
Participants	6	6		

Notes:

[25] - Maternal ITT Population

[26] - Maternal ITT Population

### Statistical analyses

<b>Statistical analysis title</b>	Statistical analysis 1
Comparison groups	Atosiban v Retosiban
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.525
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	5.15

### Secondary: Number of participants with births ≤ 24 hours from the first study treatment

End point title	Number of participants with births ≤ 24 hours from the first study treatment
End point description: Number of participants who delivered in less than or equal to 24 hours from first dose of study treatment has been presented.	
End point type	Secondary
End point timeframe: Up to 24 hours	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[27]</sup>	50 <sup>[28]</sup>		
Units: Participants				
Participants	3	6		

Notes:

[27] - Maternal ITT Population

[28] - Maternal ITT Population

### Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Atosiban v Retosiban
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4682
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	2.58

### Secondary: Number of maternal participants with non-serious adverse events (AEs) and serious adverse events (SAEs)

End point title	Number of maternal participants with non-serious adverse events (AEs) and serious adverse events (SAEs)
End point description:	
An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose: results in death; is life threatening; requires hospitalization or prolongation of existing hospitalization; results in disability/incapacity; is a congenital anomaly/birth defect; important medical events that may require medical or surgical intervention to prevent one of the other outcomes described before; is associated with liver injury and impaired liver function. Maternal Safety Population comprised of all mothers randomly assigned to treatment who have been exposed to study treatment. The number of maternal participants who experienced at least one non-serious AE and one SAE has been presented.	
End point type	Secondary
End point timeframe:	
Up to 6 weeks after delivery	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[29]</sup>	50 <sup>[30]</sup>		
Units: Participants				
Non-serious AE	34	25		
SAE	7	9		

Notes:

[29] - Maternal Safety Population

[30] - Maternal Safety Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in diastolic blood pressure (DBP) and systolic blood pressure (SBP) in maternal participants

End point title	Change from Baseline in diastolic blood pressure (DBP) and systolic blood pressure (SBP) in maternal participants
End point description:	
SBP and DBP were measured during inpatient randomized treatment phase (15 to 30 minutes, 4 to 8 hours, and 20 to 24 hours after the start of the infusion, at the end of the infusion) and at the post-infusion assessment. Baseline is the last available assessment prior to first dose of study treatment. Change from Baseline is the post-dose visit value minus Baseline. Only those participants with data available at the specified data points were analyzed (represented by n=X in category title).	
End point type	Secondary
End point timeframe:	
Baseline and up to 1 week	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[31]</sup>	50 <sup>[32]</sup>		
Units: Millimeter of mercury (mmHg)				
arithmetic mean (standard deviation)				
DBP; Day 1: 15 to 30 minutes, n=42,45	-3.6 (± 10.96)	-0.7 (± 8.95)		
DBP; Day 1: 4 to 8 hours, n=42,43	-4.3 (± 11.07)	-3.7 (± 10.28)		
DBP; Day 1: 20 to 24 hours, n=38,41	-5.7 (± 9.31)	-4.1 (± 9.90)		
DBP; Day 2, n=40,42	-4.4 (± 9.57)	-2.6 (± 9.93)		
DBP; Post-infusion assessment, n=35,41	-1.6 (± 8.63)	1.3 (± 10.12)		
SBP; Day 1: 15 to 30 minutes, n=42,45	-2.5 (± 9.53)	-0.4 (± 11.02)		
SBP; Day 1: 4 to 8 hours, n=42,43	-4.3 (± 9.05)	-3.3 (± 12.21)		
SBP; Day 1: 20 to 24 hours, n=38,41	-4.1 (± 10.16)	-5.2 (± 13.03)		
SBP; Day 2, n=40,42	-3.9 (± 11.53)	-3.0 (± 11.35)		
SBP; Post-infusion assessment, n=35,41	-1.5 (± 11.04)	-2.1 (± 11.37)		

Notes:

[31] - Maternal Safety Population

[32] - Maternal Safety Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in heart rate in maternal participants

End point title	Change from Baseline in heart rate in maternal participants
End point description:	
Heart rate was measured during inpatient randomized treatment phase (15 to 30 minutes, 4 to 8 hours, and 20 to 24 hours after the start of the infusion, at the end of the infusion) and at the post-infusion assessment. Baseline is the last available assessment prior to first dose of study treatment. Change from Baseline is the post-dose visit value minus Baseline. Only those participants with data available at the specified data points were analyzed (represented by n=X in category title).	
End point type	Secondary
End point timeframe:	
Baseline and up to 1 week	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[33]</sup>	50 <sup>[34]</sup>		
Units: Beats per minute				
arithmetic mean (standard deviation)				
Day 1: 15 to 30 minutes, n=42,46	-3.0 (± 12.65)	-0.8 (± 10.45)		
Day 1: 4 to 8 hours, n=42, 43	-5.0 (± 13.69)	-3.0 (± 13.65)		
Day 1: 20 to 24 hours, n=38, 41	-1.2 (± 14.44)	-3.1 (± 13.82)		
Day 2, n=39, 41	-2.2 (± 11.81)	-2.3 (± 13.44)		
Post-infusion assessment, n=35, 41	-2.7 (± 12.90)	-1.8 (± 13.83)		

Notes:

[33] - Maternal Safety Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change from Baseline in respiratory rate in maternal participants**

End point title	Change from Baseline in respiratory rate in maternal participants
End point description: Respiratory rate was measured during inpatient randomized treatment phase (15 to 30 minutes, 4 to 8 hours, and 20 to 24 hours after the start of the infusion, at the end of the infusion) and at the post-infusion assessment. Baseline is the last available assessment prior to first dose of study treatment. Change from Baseline is the post-dose visit value minus Baseline. Only those participants with data available at the specified data points were analyzed (represented by n=X in category title).	
End point type	Secondary
End point timeframe: Baseline and up to 1 week	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[35]</sup>	50 <sup>[36]</sup>		
Units: breaths per minute				
arithmetic mean (standard deviation)				
Day 1: 15 to 30 minutes, n=25, 28	0.3 (± 2.82)	-0.6 (± 1.93)		
Day 1: 4 to 8 hours, n=23, 24	0.0 (± 1.65)	-0.8 (± 2.33)		
Day 1: 20 to 24 hours, n=21, 21	0.2 (± 1.87)	-0.6 (± 2.40)		
Day 2, n=23, 24	-0.3 (± 1.64)	0.2 (± 3.45)		
Post-infusion assessment, n=22, 23	-0.3 (± 2.15)	-1.3 (± 2.70)		

Notes:

[35] - Maternal Safety Population

[36] - Maternal Safety Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change from Baseline in temperature in maternal participants**

End point title	Change from Baseline in temperature in maternal participants
End point description: Temperature was measured during inpatient randomized treatment phase (15 to 30 minutes, 4 to 8 hours, and 20 to 24 hours after the start of the infusion, at the end of the infusion) and at the post-infusion assessment. Baseline is the last available assessment prior to first dose of study treatment. Change from Baseline is the post-dose visit value minus Baseline. Only those participants with data available at the specified data points were analyzed (represented by n=X in category title).	
End point type	Secondary

End point timeframe:

Baseline and up to 1 week

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[37]</sup>	50 <sup>[38]</sup>		
Units: degree Celsius				
arithmetic mean (standard deviation)				
Day 1: 15 to 30 minutes, n=41, 43	-0.02 (± 0.379)	0.02 (± 0.467)		
Day 1: 4 to 8 hours, n=40, 42	-0.06 (± 0.359)	0.00 (± 0.507)		
Day 1: 20 to 24 hours, n=37, 41	-0.07 (± 0.366)	-0.03 (± 0.486)		
Day 2, n=40, 42	-0.07 (± 0.467)	-0.06 (± 0.353)		
Post-infusion assessment, n=35, 41	-0.18 (± 0.334)	-0.20 (± 0.422)		

Notes:

[37] - Maternal Safety Population

[38] - Maternal Safety Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in basophils, eosinophils, lymphocytes, monocytes, neutrophils, platelets and leukocytes count in maternal participants

End point title	Change from Baseline in basophils, eosinophils, lymphocytes, monocytes, neutrophils, platelets and leukocytes count in maternal participants
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End point description:

Blood samples were collected for the evaluation of change in basophils, eosinophils, lymphocytes, monocytes, neutrophils, platelets and leukocytes count. Baseline is defined as the last available assessment prior to the first dose of study treatment. Change from Baseline is the post-dose visit value minus Baseline. Only those participants with data available at the specified data points were analyzed (represented by n=X in category title). 99999 indicates standard deviation was not calculable for a single data point.

End point type	Secondary
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End point timeframe:

Baseline and up to 1 week

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[39]</sup>	50 <sup>[40]</sup>		
Units: Billion cells per liter (L)				
arithmetic mean (standard deviation)				
Basophils;Day2,n=21,23	0.003 (± 0.0362)	0.010 (± 0.0304)		

Basophils;Post-infusion assessment,n=24,28	0.001 (± 0.0315)	0.007 (± 0.0181)		
Basophils;early withdrawal,n=1,1	-0.020 (± 99999)	0.030 (± 99999)		
Eosinophils;Day2,n=21,23	-0.010 (± 0.0626)	-0.037 (± 0.1181)		
Eosinophils;Post-infusion assessment,n=24,28	0.023 (± 0.0442)	0.066 (± 0.1535)		
Eosinophils;early withdrawal,n=1,1	0.030 (± 99999)	0.050 (± 99999)		
Lymphocytes;Day2,n=21,23	0.186 (± 0.9115)	0.067 (± 0.6017)		
Lymphocytes;Post-infusion assessment,n=24,28	0.348 (± 0.8611)	0.233 (± 0.8047)		
Lymphocytes;early withdrawal,n=1,1	0.270 (± 99999)	-1.770 (± 99999)		
Monocytes;Day2,n=21,23	0.082 (± 0.2222)	0.044 (± 0.2702)		
Monocytes;Post-infusion assessment,n=24,28	0.222 (± 0.1904)	0.133 (± 0.3467)		
Monocytes;early withdrawal,n=1,1	-0.160 (± 99999)	0.410 (± 99999)		
Neutrophils;Day2,n=21,23	0.102 (± 2.6712)	0.559 (± 3.3890)		
Neutrophils;Post-infusion assessment,n=24,28	-1.865 (± 2.9246)	-0.670 (± 2.7063)		
Neutrophils;early withdrawal,n=1,1	-0.710 (± 99999)	-3.550 (± 99999)		
Platelets;Day2,n=22,25	0.0 (± 25.95)	-2.4 (± 36.59)		
Platelets;Post-infusion assessment,n=24,31	21.5 (± 63.14)	20.6 (± 43.74)		
Platelets;early withdrawal,n=1,1	-33.0 (± 99999)	-58.0 (± 99999)		
Leukocytes;Day2,n=23,25	0.17 (± 2.785)	0.72 (± 2.905)		
Leukocytes;Post-infusion assessment,n=25,30	-1.18 (± 2.492)	-0.05 (± 2.756)		
Leukocytes;early withdrawal,n=1,1	-0.60 (± 99999)	-4.80 (± 99999)		

Notes:

[39] - Maternal Safety Population

[40] - Maternal Safety Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in erythrocytes in maternal participants

End point title	Change from Baseline in erythrocytes in maternal participants
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End point description:

Blood samples were collected for the evaluation of change in erythrocytes from Baseline. Baseline is defined as the last available assessment prior to the first dose of study treatment. Change from Baseline is the post-dose visit value minus Baseline. Only those participants with data available at the specified data points were analyzed (represented by n=X in category title). 99999 indicates standard deviation was not calculable for a single data point.

End point type	Secondary
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End point timeframe:

Baseline and up to 1 week

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[41]</sup>	50 <sup>[42]</sup>		
Units: Trillion cells per liter				
arithmetic mean (standard deviation)				
Day 2, n=23, 27	-0.22 (± 0.284)	-0.29 (± 0.261)		
Post-infusion assessment, n=25, 31	0.06 (± 0.257)	0.05 (± 0.236)		
Early withdrawal, n =1, 1	-0.20 (± 99999)	-0.70 (± 99999)		

Notes:

[41] - Maternal Safety Population

[42] - Maternal Safety Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in hemoglobin and Erythrocyte Mean Corpuscular hemoglobin Concentration (MCHC) in maternal participants

End point title	Change from Baseline in hemoglobin and Erythrocyte Mean Corpuscular hemoglobin Concentration (MCHC) in maternal participants
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End point description:

Blood samples were collected for the evaluation of change in hemoglobin levels and MCHC from Baseline. Baseline is defined as the last available assessment prior to the first dose of study treatment. Change from Baseline is the post-dose visit value minus. 99999 indicates standard deviation was not calculable for a single data point.

End point type	Secondary
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End point timeframe:

Baseline and up to 1 week

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[43]</sup>	50 <sup>[44]</sup>		
Units: grams per liter (g/L)				
arithmetic mean (standard deviation)				
Hemoglobin; Day2, n=23, 27	-5.4 (± 7.81)	-8.4 (± 6.86)		
Hemoglobin; Post-infusion assessment, n=25, 31	0.8 (± 7.55)	0.5 (± 5.37)		
Hemoglobin; early withdrawal, n=1, 1	-8.0 (± 99999)	-19.0 (± 99999)		
MCHC; Day 2, n=23, 27	1.0 (± 9.41)	0.9 (± 6.85)		
MCHC; Post-infusion assessment, n=25, 31	1.0 (± 7.36)	0.4 (± 8.98)		
MCHC; early withdrawal, n=1, 1	-3.0 (± 99999)	24.0 (± 99999)		



Notes:

[43] - Maternal Safety Population

[44] - Maternal Safety Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in erythrocyte mean corpuscular volume (MCV) and mean platelet volume (MPV) in maternal participants

End point title	Change from Baseline in erythrocyte mean corpuscular volume (MCV) and mean platelet volume (MPV) in maternal participants
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End point description:

Blood samples were collected for the evaluation of change in MCV and MPV from Baseline. Baseline is defined as the last available assessment prior to the first dose of study treatment. Change from Baseline is the post-dose visit value minus Baseline. Only those participants with data available at the specified data points were analyzed (represented by n=X in category title). 99999 indicates standard deviation was not calculable for a single data point.

End point type	Secondary
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End point timeframe:

Baseline and up to 1 week

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[45]</sup>	50 <sup>[46]</sup>		
Units: femtoliter (fL)				
arithmetic mean (standard deviation)				
MCV; Day 2, n=23, 27	0.3 (± 2.67)	-0.4 (± 1.82)		
MCV; Post-infusion assessment, n=25, 31	-1.2 (± 2.17)	-1.0 (± 2.22)		
MCV; early withdrawal, n=1, 1	-1.0 (± 99999)	-5.0 (± 99999)		
MPV; Day 2, n=22, 25	0.05 (± 0.607)	0.06 (± 0.553)		
MPV, Post-infusion assessment, n=24, 31	-0.10 (± 0.639)	-0.03 (± 0.803)		
MPV, early withdrawal, n=1, 1	0.00 (± 99999)	-1.40 (± 99999)		

Notes:

[45] - Maternal Safety Population

[46] - Maternal Safety Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transferase (GGT) and lactate dehydrogenase (LDH) levels in maternal participants

End point title	Change from Baseline in alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST),
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## End point description:

Blood samples were collected for the evaluation of change in ALP, ALT, AST, GGT and LDH from Baseline. Baseline is defined as the last available assessment prior to the first dose of study treatment. Change from Baseline is the post-dose visit value minus Baseline. Only those participants with data available at the specified data points were analyzed (represented by n=X in category title). 99999 indicates standard deviation was not calculable for a single data point.

End point type	Secondary
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## End point timeframe:

Baseline and up to 1 week
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End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[47]</sup>	50 <sup>[48]</sup>		
Units: International Units per liter (IU/L)				
arithmetic mean (standard deviation)				
ALP; Day 2, n=35, 35	-10.1 (± 12.12)	-12.6 (± 13.07)		
ALP; Post-infusion assessment, n=30, 35	14.1 (± 39.85)	5.9 (± 15.87)		
ALP; early withdrawal, n=1, 1	-6.0 (± 99999)	-19.0 (± 99999)		
AST; Day 2, n=34, 35	-0.9 (± 4.82)	-1.7 (± 3.07)		
AST; Post-infusion assessment, n=29, 35	-1.3 (± 4.87)	-1.3 (± 4.09)		
AST; early withdrawal, n=1, 1	-3.0 (± 99999)	1.0 (± 99999)		
ALT; Day 2, n= 35, 35	-0.2 (± 2.53)	0.0 (± 2.40)		
ALT; Post-infusion assessment, n= 30, 35	0.0 (± 6.34)	0.8 (± 6.19)		
ALT; early withdrawal, n= 1, 1	-2.0 (± 99999)	5.0 (± 99999)		
GGT; Day 2, n= 35, 35	-0.4 (± 2.44)	-0.9 (± 3.08)		
GGT; Post-infusion assessment, n=30, 35	17.6 (± 79.05)	2.3 (± 4.39)		
GGT; early withdrawal, n=1, 1	0.0 (± 99999)	0.0 (± 99999)		
LDH; Day 2, n=34, 35	-9.7 (± 50.58)	-20.0 (± 29.18)		
LDH; Post-infusion assessment, n=29, 35	-2.4 (± 22.08)	-5.4 (± 30.93)		
LDH; early withdrawal, n=1, 1	-18.0 (± 99999)	-59.0 (± 99999)		

## Notes:

[47] - Maternal Safety Population

[48] - Maternal Safety Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in albumin and protein levels in maternal participants

End point title	Change from Baseline in albumin and protein levels in maternal participants
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**End point description:**

Blood samples were collected for the evaluation of change in albumin and protein levels from Baseline. Baseline is defined as the last available assessment prior to the first dose of study treatment. Change from Baseline is the post-dose visit value minus Baseline. Only those participants with data available at the specified data points were analyzed (represented by n=X in category title). 99999 indicates standard deviation was not calculable for a single data point.

End point type	Secondary
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**End point timeframe:**

Baseline and up to 1 week

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[49]</sup>	50 <sup>[50]</sup>		
Units: grams per liter (g/L)				
arithmetic mean (standard deviation)				
Albumin; Day 2, n=35, 35	-1.9 (± 2.28)	-2.0 (± 1.95)		
Albumin; Post-infusion assessment, n=30, 35	0.3 (± 2.39)	-0.2 (± 2.26)		
Albumin; early withdrawal, n=1, 1	-4.0 (± 99999)	-8.0 (± 99999)		
Protein; Day 2, n=35, 35	-3.7 (± 4.18)	-3.3 (± 3.69)		
Protein; Post-infusion assessment, n=30, 35	0.5 (± 4.73)	0.0 (± 4.05)		
Protein; early withdrawal, n=1, 1	-5.0 (± 99999)	-12.0 (± 99999)		

**Notes:**

[49] - Maternal Safety Population

[50] - Maternal Safety Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change from Baseline in calcium, chloride, carbon dioxide, glucose, potassium, magnesium, phosphate and sodium level in maternal participants**

End point title	Change from Baseline in calcium, chloride, carbon dioxide, glucose, potassium, magnesium, phosphate and sodium level in maternal participants
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**End point description:**

Blood samples were collected for the evaluation of change from Baseline in levels of calcium, chloride, carbon dioxide, glucose, potassium, magnesium, phosphate, and sodium. Baseline is defined as the last available assessment prior to the first dose of study treatment. Change from Baseline is the post-dose visit value minus Baseline. Only those participants with data available at the specified data points were analyzed (represented by n=X in category title). 99999 indicates standard deviation was not calculable for a single data point.

End point type	Secondary
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**End point timeframe:**

Baseline and up to 1 week

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[51]</sup>	50 <sup>[52]</sup>		
Units: millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
Calcium; Day 2, n=34, 35	-0.097 (± 0.1125)	-0.078 (± 0.0884)		
Calcium; Post-infusion assessment, n=29, 35	0.018 (± 0.0953)	0.023 (± 0.0861)		
Calcium; early withdrawal, n=1, 1	-0.120 (± 99999)	-0.230 (± 99999)		
Chloride; Day 2, n=35, 35	1.5 (± 2.02)	1.4 (± 2.03)		
Chloride; Post-infusion assessment, n=30, 35	-1.5 (± 1.83)	-1.3 (± 2.63)		
Chloride; early withdrawal, n=1, 1	2.0 (± 99999)	8.0 (± 99999)		
Carbon dioxide; Day 2, n=34, 35	0.7 (± 2.34)	0.3 (± 2.63)		
Carbon dioxide, Post-infusion assessment, n=29,35	1.9 (± 2.06)	1.9 (± 2.67)		
Carbon dioxide, early withdrawal, n=1, 1	-2.0 (± 99999)	6.0 (± 99999)		
Glucose; Day 2, n=35,35	0.13 (± 2.013)	1.51 (± 2.156)		
Glucose; Post-infusion assessment, n=30, 35	-0.70 (± 1.994)	-0.35 (± 2.283)		
Glucose; early withdrawal, n= 1, 1	0.70 (± 99999)	-5.20 (± 99999)		
Potassium; Day 2, n= 34, 35	0.06 (± 0.392)	-0.06 (± 0.346)		
Potassium; Post-infusion assessment, n= 29, 35	0.21 (± 0.362)	0.18 (± 0.355)		
Potassium; early withdrawal, n= 1,1	-0.10 (± 99999)	0.50 (± 99999)		
Magnesium; Day 2, n= 35,35	0.073 (± 0.2098)	-0.003 (± 0.0657)		
Magnesium, Post-infusion assessment, n= 30,35	0.026 (± 0.0760)	0.009 (± 0.0772)		
Magnesium; early withdrawal, n= 1,1	-0.060 (± 99999)	0.030 (± 99999)		
Phosphate; Day 2, n= 35,35	-0.101 (± 0.2684)	-0.170 (± 0.2357)		
Phosphate; Post-infusion assessment, n= 30,35	0.041 (± 0.2267)	0.094 (± 0.2864)		
Phosphate; early withdrawal, n= 1,1	0.100 (± 99999)	-0.120 (± 99999)		
Sodium; Day 2, n= 35,35	0.7 (± 2.13)	0.1 (± 1.69)		
Sodium; Post-infusion assessment, n= 30,35	-1.1 (± 2.05)	-0.2 (± 2.11)		
Sodium; early withdrawal, n= 1,1	-1.0 (± 99999)	3.0 (± 99999)		

Notes:

[51] - Maternal Safety Population

[52] - Maternal Safety Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in direct bilirubin, bilirubin, indirect bilirubin, creatinine and urate levels in maternal participants

End point title	Change from Baseline in direct bilirubin, bilirubin, indirect
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## End point description:

Blood samples were collected for the evaluation of change from Baseline in levels of direct bilirubin, bilirubin, indirect bilirubin, creatinine and urate. Baseline is defined as the last available assessment prior to the first dose of study treatment. Change from Baseline is the post-dose visit value minus Baseline. Only those participants with data available at the specified data points were analyzed (represented by n=X in category title). 99999 indicates standard deviation was not calculable for a single data point.

End point type Secondary

End point timeframe:

Baseline and up to 1 week

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[53]</sup>	50 <sup>[54]</sup>		
Units: micromoles per liter (µmol/L)				
arithmetic mean (standard deviation)				
Direct Bilirubin; Day2, n=35,35	-0.3 (± 0.85)	-0.3 (± 0.66)		
Post-infusion assessment, n=30,35	-0.5 (± 3.41)	-0.1 (± 0.73)		
Direct Bilirubin;early withdrawal, n=1,1	0.0 (± 99999)	0.0 (± 99999)		
Bilirubin;Day2, n= 35,35	-0.7 (± 2.52)	-1.3 (± 2.03)		
Bilirubin; Post-infusion assessment, n= 30, 35	-1.1 (± 8.24)	-0.5 (± 2.01)		
Bilirubin; early withdrawal, n= 1,1	-2.0 (± 99999)	-3.0 (± 99999)		
Indirect Bilirubin; Day2, n=35,35	-0.4 (± 2.35)	-1.1 (± 1.98)		
Indirect Bilirubin;Postinfusion assessment,n=30,35	-0.6 (± 5.06)	-0.4 (± 2.03)		
Indirect Bilirubin; early withdrawal, n=1,1	-2.0 (± 99999)	-3.0 (± 99999)		
Creatinine; Day2, n=35,34	1.75 (± 6.765)	0.04 (± 5.336)		
Creatinine; Post-infusion assessment, n=30,33	2.19 (± 4.437)	0.72 (± 4.680)		
Creatinine; early withdrawal, n=1,1	-0.90 (± 99999)	-6.10 (± 99999)		

Notes:

[53] - Maternal Safety Population

[54] - Maternal Safety Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of maternal participants with AEs of special interest (AESI)

End point title Number of maternal participants with AEs of special interest (AESI)

End point description:

Maternal AESI included: maternal death; chorioamnionitis and its complications (clinical chorioamnionitis, preterm premature rupture of membranes, endomyometritis, wound infection, pelvic abscess, bacteremia, septic shock, disseminated intravascular coagulation, and adult RDS); placental abruption; postpartum hemorrhage – postpartum hemorrhage and/or retained placenta and pulmonary edema. The number of participants with at least one AESI has been presented.

End point type Secondary

End point timeframe:  
Up to 6 weeks post-delivery

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[55]</sup>	50 <sup>[56]</sup>		
Units: Participants				
Participants	4	7		

Notes:

[55] - Maternal Safety Population

[56] - Maternal Safety Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of maternal participants with disease related AEs (DRE)

End point title	Number of maternal participants with disease related AEs (DRE)
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End point description:

Maternal DREs included: signs and symptoms of labor discomfort (example, cramping, backache, muscle aches, nausea); subsequent episodes of preterm labor and hospitalization for delivery. The number of participants with at least one DRE has been presented.

End point type	Secondary
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End point timeframe:

Up to 6 weeks post-delivery

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[57]</sup>	50 <sup>[58]</sup>		
Units: Participants				
Participants	5	5		

Notes:

[57] - Maternal Safety Population

[58] - Maternal Safety Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with fetal non-serious AEs and SAEs

End point title	Number of participants with fetal non-serious AEs and SAEs
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End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose: results in death; is life threatening; requires hospitalization or prolongation of existing hospitalization; results in disability/incapacity; is a congenital anomaly/birth defect; important medical events that may require medical or surgical

intervention to prevent one of the other outcomes described before; is associated with liver injury and impaired liver function. The number of participants who experienced at least one non-serious AE and one SAE has been presented.

End point type	Secondary
End point timeframe:	
Up to 17 weeks	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[59]</sup>	50 <sup>[60]</sup>		
Units: Participants				
Non-serious AE	6	6		
SAE	4	2		

Notes:

[59] - Maternal Safety Population

[60] - Maternal Safety Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with fetal AESI

End point title	Number of participants with fetal AESI
End point description:	
Fetal AESI included: intrauterine fetal demise; category II or III fetal heart rate tracing; and fetal inflammatory response syndrome characterized by cord blood interleukin-6 >11 picogram per milliliter (pg/mL), funisitis, or chorionic vasculitis. The number of participants who experienced at least one AESI has been presented.	
End point type	Secondary
End point timeframe:	
Up to 17 weeks	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[61]</sup>	50 <sup>[62]</sup>		
Units: Participants				
Participants	5	5		

Notes:

[61] - Maternal Safety Population

[62] - Maternal Safety Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Neonatal APGAR Scores

End point title	Neonatal APGAR Scores
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End point description:

APGAR is a quick test to assess the health of new born children. The test is performed at 1 and 5 minutes after birth. APGAR scale is determined by evaluating the new born on five categories (appearance, pulse, grimace, activity and respiration) on a scale from zero to two, then summing up the five values obtained. APGAR score ranges from 0 to 10 where a score of 7 and above is normal. The mean and standard deviation of APGAR scores at one minute and at five minutes of birth has been presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary
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End point timeframe:

Up to 5 minutes after birth

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[63]</sup>	50 <sup>[64]</sup>		
Units: Score on APGAR scale				
arithmetic mean (standard deviation)				
one minute, n=46, 50	8.2 (± 1.35)	8.4 (± 1.14)		
five minutes, n=46, 50	9.1 (± 0.96)	9.4 (± 0.67)		

Notes:

[63] - Neonatal ITT Population

[64] - Neonatal ITT Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Weight of neonates

End point title	Weight of neonates
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End point description:

The weight of neonates was obtained from the neonate birth record. The mean weight of neonates and standard deviation has been presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary
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End point timeframe:

Up to 17 weeks

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46 <sup>[65]</sup>	49 <sup>[66]</sup>		
Units: grams (g)				
arithmetic mean (standard deviation)				
grams (g)	2761.9 (± 567.84)	2844.4 (± 664.80)		

Notes:

[65] - Neonatal ITT Population

[66] - Neonatal ITT Population



## Statistical analyses

No statistical analyses for this end point

### Secondary: Head circumference of neonates

End point title	Head circumference of neonates
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End point description:

The head circumference was determined from the neonate birth record. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary
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End point timeframe:

Up to 17 weeks

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43 <sup>[67]</sup>	42 <sup>[68]</sup>		
Units: centimeters (cm)				
arithmetic mean (standard deviation)				
centimeters (cm)	32.95 (± 2.179)	33.00 (± 1.892)		

Notes:

[67] - Neonatal ITT Population

[68] - Neonatal ITT Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of neonatal participants with non-serious AEs and SAEs

End point title	Number of neonatal participants with non-serious AEs and SAEs
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End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose: results in death; is life threatening; requires hospitalization or prolongation of existing hospitalization; results in disability/incapacity; is a congenital anomaly/birth defect; important medical events that may require medical or surgical intervention to prevent one of the other outcomes described before; is associated with liver injury and impaired liver function. The number of participants who experienced at least one non-serious AE and one SAE has been presented. Neonatal Safety Population consisted of neonates whose mothers received randomized treatment.

End point type	Secondary
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End point timeframe:

Up to 28 days after the EDD of 40 weeks gestation

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[69]</sup>	50 <sup>[70]</sup>		
Units: Participants				
Non-serious AEs	23	17		
SAEs	10	11		

Notes:

[69] - Neonatal Safety Population

[70] - Neonatal Safety Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of neonatal participants with AESI

End point title	Number of neonatal participants with AESI
End point description:	
Neonatal AESI included: Neonatal death; Asphyxia; Infections (early onset neonatal sepsis, septic shock, pneumonia, meningitis); RDS; Hypotension; IVH/periventricular leukomalacia; Bronchopulmonary dysplasia; Neonatal acidosis; Hyperbilirubinemia; Necrotizing enterocolitis; and Hypoxic ischemic encephalopathy. The number of neonatal participants who experienced at least one AESI has been presented.	
End point type	Secondary
End point timeframe:	
Up to 28 days after EDD of 40 weeks gestation	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[71]</sup>	50 <sup>[72]</sup>		
Units: Participants				
Participants	19	16		

Notes:

[71] - Neonatal Safety Population

[72] - Neonatal Safety Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of neonatal participants with DRE

End point title	Number of neonatal participants with DRE
End point description:	
The disease related neonatal events occurring in Infants born prior to 37 completed weeks included: apnea (severe), respiratory failure due to fatigue, hypoxia, or air leak from alveolar injury, patent ductus arteriosus, bradycardia, ventriculomegaly, cerebellar hemorrhage, hydrocephalus other than congenital, gastroesophageal reflux, aspiration pneumonia, anemia, retinopathy of prematurity (all stages), hearing disorder, temperature instability and hypoglycemia. The number of participants with at least one DRE has been presented.	
End point type	Secondary
End point timeframe:	
Up to 28 days after EDD of 40 weeks gestation	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[73]</sup>	50 <sup>[74]</sup>		
Units: Participants				
Participants	5	3		

Notes:

[73] - Neonatal Safety Population

[74] - Neonatal Safety Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Maternal length of stay in hospital

End point title	Maternal length of stay in hospital
End point description: The length of hospital stay associated with hospital admission for preterm labor and term labor/term delivery was collected from review of medical records. Only those participants with data available at the specified data points were analyzed (represented by n=X in category title).	
End point type	Secondary
End point timeframe: Up to 28 days post EDD (40 0/7 weeks gestation)	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[75]</sup>	50 <sup>[76]</sup>		
Units: Days				
median (full range (min-max))				
Preterm labor, n=13, 10	5.549 (1.32 to 72.00)	7.487 (0.87 to 37.82)		
Term labor, n=25, 28	3.146 (0.17 to 62.71)	3.398 (0.41 to 36.74)		

Notes:

[75] - Maternal Safety Population

[76] - Maternal Safety Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants admitted to particular hospital unit

End point title	Number of participants admitted to particular hospital unit
End point description: Maternal healthcare resource utilization associated with an episode of preterm labor and normal term delivery were collected from the review of medical records. The number of participants who were admitted to a particular hospital unit like general ward, private/semi-private room, recovery, and other has been presented.	

End point type	Secondary
End point timeframe:	
Up to 28 days post EDD (40 0/7 weeks gestation)	

End point values	Retosiban	Atosiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47 <sup>[77]</sup>	50 <sup>[78]</sup>		
Units: Participants				
Preterm labor, general ward	9	7		
Preterm labor, private/semi-private room	1	0		
Preterm, Other	3	4		
Normal term labor, general ward	16	12		
Normal term labor, ward-not specified	2	0		
Normal term labor,private/semi-private room	1	7		
Normal term labor, recovery	1	2		
Normal term labor, Other	5	7		

Notes:

[77] - Maternal Safety Population

[78] - Maternal Safety Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Retosiban clearance

End point title	Retosiban clearance
End point description:	
Maternal blood samples were collected at the indicated time points for pharmacokinetic analysis. Data is a combined data set. Data is presented for 10 participants from retosiban arm of study 200719 (NCT02377466) and 43 participants from retosiban arm of study 200721 (NCT02292771).	
End point type	Secondary
End point timeframe:	
Day 1 (2 to 4 hours, 10 to 14 hours) and Day 2 (22 to 26 hours, and 48 to 54 hours) post-infusion	

End point values	Retosiban			
Subject group type	Subject analysis set			
Number of subjects analysed	53 <sup>[79]</sup>			
Units: Microgram per liter				
geometric mean (geometric coefficient of variation)	83.4 (± 5.25)			

Notes:

[79] - Maternal Safety Population. Number of participants is combined from 2 studies. Actual value is 53.

### Statistical analyses

No statistical analyses for this end point

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**Secondary: Volume of distribution of retosiban**

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End point title	Volume of distribution of retosiban
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End point description:

Maternal blood samples were collected at the indicated time points for pharmacokinetic analysis. Data is a combined data set. Data is presented for 10 participants from retosiban arm of study 200719 (NCT02377466) and 43 participants from retosiban arm of study 200721 (NCT02292771).

End point type	Secondary
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End point timeframe:

Day 1 (2 to 4 hours, 10 to 14 hours) and Day 2 (22 to 26 hours, and 48 to 54 hours) post-infusion

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End point values	Retosiban			
Subject group type	Subject analysis set			
Number of subjects analysed	53 <sup>[80]</sup>			
Units: Microgram per liter				
geometric mean (geometric coefficient of variation)	68.6 (± 109)			

Notes:

[80] - Maternal Safety Population. Number of participants is combined from 2 studies. Actual value is 53.

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**Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the start of study treatment and until Day 894

Adverse event reporting additional description:

SAEs and AEs were analyzed in Maternal Safety Population and Neonatal Safety Population which comprised of mothers randomly assigned to treatment who were exposed to study treatment and neonates whose mothers received randomized treatment. One participant was withdrawn prior to delivery and was not included in the summary.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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### Reporting groups

Reporting group title	Retosiban (Maternal)
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Reporting group description:

Participants were administered 6 milligram (mg) IV loading dose of retosiban over 5 minutes followed by a 6 milligram per hour (mg/hour) continuous infusion of retosiban over 48 hours. Participants with an inadequate response any time after first hour of treatment were administered another 6 mg retosiban loading dose followed by 12 mg/hour continuous infusion for remainder of 48-hour treatment period.

Reporting group title	Atosiban (Maternal)
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Reporting group description:

Participants were administered atosiban in 3 successive stages. An initial bolus dose of 6.75 mg using atosiban 6.75 mg/0.9 milliliter (mL) solution for injection, followed by continuous high dose infusion at 18 mg/hour for 3 hours, then a lower 6 mg/hour infusion for the remainder of the 48-hour using the atosiban 37.5 mg/5 mL concentrate for solution.

Reporting group title	Retosiban (Fetal)
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Reporting group description:

Participants were administered 6 milligram (mg) IV loading dose of retosiban over 5 minutes followed by a 6 milligram per hour (mg/hour) continuous infusion of retosiban over 48 hours. Participants with an inadequate response any time after first hour of treatment were administered another 6 mg retosiban loading dose followed by 12 mg/hour continuous infusion for remainder of 48-hour treatment period.

Reporting group title	Atosiban (Fetal)
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Reporting group description:

Participants were administered atosiban in 3 successive stages. An initial bolus dose of 6.75 mg using atosiban 6.75 mg/0.9 milliliter (mL) solution for injection, followed by continuous high dose infusion at 18 mg/hour for 3 hours, then a lower 6 mg/hour infusion for the remainder of the 48-hour using the atosiban 37.5 mg/5 mL concentrate for solution.

Reporting group title	Retosiban (Neonatal)
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Reporting group description:

Participants were administered 6 milligram (mg) IV loading dose of retosiban over 5 minutes followed by a 6 milligram per hour (mg/hour) continuous infusion of retosiban over 48 hours. Participants with an inadequate response any time after first hour of treatment were administered another 6 mg retosiban loading dose followed by 12 mg/hour continuous infusion for remainder of 48-hour treatment period.

Reporting group title	Atosiban (Neonatal)
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Reporting group description:

Participants were administered atosiban in 3 successive stages. An initial bolus dose of 6.75 mg using atosiban 6.75 mg/0.9 milliliter (mL) solution for injection, followed by continuous high dose infusion at 18 mg/hour for 3 hours, then a lower 6 mg/hour infusion for the remainder of the 48-hour using the atosiban 37.5 mg/5 mL concentrate for solution.

<b>Serious adverse events</b>	Retosiban (Maternal)	Atosiban (Maternal)	Retosiban (Fetal)
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 47 (14.89%)	9 / 50 (18.00%)	4 / 47 (8.51%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Foetal monitoring abnormal			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Injury, poisoning and procedural complications			
Abdominal wound dehiscence			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (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, familial and genetic disorders			
Congenital hydronephrosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Ankyloglossia congenital			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Atrial septal defect			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Cataract congenital			

subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Pyloric stenosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Ventricular septal defect			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Cardiac disorders			
Foetal heart rate disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal heart rate deceleration abnormality			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Postpartum haemorrhage			
subjects affected / exposed	0 / 47 (0.00%)	3 / 50 (6.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Preterm premature rupture of membranes			
subjects affected / exposed	1 / 47 (2.13%)	2 / 50 (4.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Normal labour			



subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (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
Pre-eclampsia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (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	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (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
Premature separation of placenta			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (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
Oligohydramnios			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrops foetalis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice neonatal			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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			
Sudden infant death syndrome			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Immune system disorders			

Milk allergy			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (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			
Abdominal pain			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (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
Pancreatitis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (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
Retroperitoneal haematoma			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (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
Gastric perforation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (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
Hyperbilirubinaemia neonatal			

subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Respiratory, thoracic and mediastinal disorders			
Neonatal respiratory distress syndrome			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Choking			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Hypoxia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Meconium aspiration syndrome			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Pneumothorax			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Infections and infestations			
Amniotic cavity infection			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (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
Appendicitis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (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

Haematoma infection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (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
Urinary tract infection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (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
Bacterial disease carrier			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Gastroenteritis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (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

<b>Serious adverse events</b>	Atosiban (Fetal)	Retosiban (Neonatal)	Atosiban (Neonatal)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 50 (4.00%)	10 / 46 (21.74%)	11 / 50 (22.00%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Investigations			
Foetal monitoring abnormal			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Abdominal wound dehiscence			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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, familial and genetic disorders			
Congenital hydronephrosis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 46 (0.00%)	0 / 50 (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
Ankyloglossia congenital			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial septal defect			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract congenital			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	0 / 50 (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
Pyloric stenosis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	0 / 50 (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
Ventricular septal defect			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	0 / 50 (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
Cardiac disorders			
Foetal heart rate disorder			

subjects affected / exposed	1 / 50 (2.00%)	0 / 46 (0.00%)	0 / 50 (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 heart rate deceleration abnormality			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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			
Postpartum haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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
Normal labour			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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
Pre-eclampsia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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 separation of placenta			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Oligohydramnios			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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
Hydrops foetalis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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
Jaundice neonatal			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	2 / 50 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Sudden infant death syndrome			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Immune system disorders			
Milk allergy			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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			
Abdominal pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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
Pancreatitis			

subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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
Retroperitoneal haematoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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
Gastric perforation			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	0 / 50 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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
Hyperbilirubinaemia neonatal			
subjects affected / exposed	0 / 50 (0.00%)	4 / 46 (8.70%)	3 / 50 (6.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Neonatal respiratory distress syndrome			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Choking			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	0 / 50 (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



Meconium aspiration syndrome			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Amniotic cavity infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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
Appendicitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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
Haematoma infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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
Postoperative wound infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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
Urinary tract infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (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
Bacterial disease carrier			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	0 / 50 (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
Gastroenteritis			

subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	0 / 50 (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

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

<b>Non-serious adverse events</b>	Retosiban (Maternal)	Atosiban (Maternal)	Retosiban (Fetal)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 47 (72.34%)	25 / 50 (50.00%)	6 / 47 (12.77%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Eyelid haemangioma			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	1 / 47 (2.13%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	1	1	0
Pregnancy, puerperium and perinatal conditions			
Foetal hypokinesia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	2 / 47 (4.26%)
occurrences (all)	1	0	2
Oligohydramnios			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Postpartum haemorrhage			
subjects affected / exposed	1 / 47 (2.13%)	2 / 50 (4.00%)	0 / 47 (0.00%)
occurrences (all)	1	2	0
Gestational hypertension			
subjects affected / exposed	1 / 47 (2.13%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	1	1	0
Polyhydramnios			

subjects affected / exposed	2 / 47 (4.26%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Premature labour			
subjects affected / exposed	2 / 47 (4.26%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Preterm premature rupture of membranes			
subjects affected / exposed	2 / 47 (4.26%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Jaundice neonatal			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Cephalhaematoma			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 47 (2.13%)	3 / 50 (6.00%)	0 / 47 (0.00%)
occurrences (all)	1	3	0
Asthenia			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			

subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 50 (2.00%) 1	0 / 47 (0.00%) 0
Suprapubic pain subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	0 / 50 (0.00%) 0	0 / 47 (0.00%) 0
Reproductive system and breast disorders			
Scrotal oedema subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	0 / 47 (0.00%) 0
Testicular retraction subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	0 / 47 (0.00%) 0
Vaginal haemorrhage subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 4	1 / 50 (2.00%) 2	0 / 47 (0.00%) 0
Breast engorgement subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 50 (2.00%) 1	0 / 47 (0.00%) 0
Uterine atony subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	0 / 50 (0.00%) 0	0 / 47 (0.00%) 0
Vulval oedema subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	0 / 50 (0.00%) 0	0 / 47 (0.00%) 0
Vulvovaginal pruritus subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	0 / 50 (0.00%) 0	0 / 47 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Neonatal respiratory distress syndrome subjects affected / exposed occurrences (all)	4 / 47 (8.51%) 4	1 / 50 (2.00%) 1	0 / 47 (0.00%) 0
Transient tachypnoea of the newborn subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	0 / 47 (0.00%) 0
Apnoea			

subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Choking			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Respiratory acidosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Respiratory disorder neonatal			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Use of accessory respiratory muscles			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 47 (4.26%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Agitation			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Mood swings			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Investigations			
Escherichia test positive			

subjects affected / exposed	2 / 47 (4.26%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Psychiatric evaluation abnormal			
subjects affected / exposed	0 / 47 (0.00%)	2 / 50 (4.00%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Candida test positive			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Klebsiella test positive			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
White blood cell count increased			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	3 / 47 (6.38%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	3	0	0
Abdominal wound dehiscence			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Congenital hydronephrosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Hydrocele			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Foetal heart rate disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Foetal heart rate deceleration			

abnormality			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	3 / 47 (6.38%)
occurrences (all)	0	0	15
Bradycardia foetal			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	1 / 47 (2.13%)	1 / 50 (2.00%)	1 / 47 (2.13%)
occurrences (all)	1	1	1
Bradycardia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Tachycardia foetal			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	3
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	8 / 47 (17.02%)	3 / 50 (6.00%)	0 / 47 (0.00%)
occurrences (all)	8	3	0
Dizziness			
subjects affected / exposed	1 / 47 (2.13%)	3 / 50 (6.00%)	0 / 47 (0.00%)
occurrences (all)	1	3	0
Burning sensation			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Polycythaemia neonatorum			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Anaemia			

subjects affected / exposed	4 / 47 (8.51%)	2 / 50 (4.00%)	0 / 47 (0.00%)
occurrences (all)	4	2	0
Anaemia of pregnancy			
subjects affected / exposed	1 / 47 (2.13%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	1	1	0
Leukocytosis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Auditory disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eyelid oedema			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Infantile colic			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	10 / 47 (21.28%)	5 / 50 (10.00%)	0 / 47 (0.00%)
occurrences (all)	12	5	0
Flatulence			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Inguinal hernia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Regurgitation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Umbilical hernia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Vomiting			



subjects affected / exposed	1 / 47 (2.13%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	1	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Abdominal rigidity			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Dental caries			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Gingival bleeding			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hyperbilirubinaemia neonatal			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Jaundice			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Hepatic steatosis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Acne infantile			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Blister			

subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	0 / 47 (0.00%) 0
Dry skin subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	0 / 47 (0.00%) 0
Macule subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	0 / 50 (0.00%) 0	0 / 47 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 50 (2.00%) 1	0 / 47 (0.00%) 0
Renal and urinary disorders Renal pain subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 50 (2.00%) 1	0 / 47 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	2 / 50 (4.00%) 2	0 / 47 (0.00%) 0
Arthralgia subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	1 / 50 (2.00%) 1	0 / 47 (0.00%) 0
Flank pain subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2	0 / 50 (0.00%) 0	0 / 47 (0.00%) 0
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 50 (2.00%) 1	0 / 47 (0.00%) 0
Neck pain subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	0 / 50 (0.00%) 0	0 / 47 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	0 / 50 (0.00%) 0	0 / 47 (0.00%) 0
Infections and infestations			

Urinary tract infection			
subjects affected / exposed	4 / 47 (8.51%)	3 / 50 (6.00%)	0 / 47 (0.00%)
occurrences (all)	4	3	0
Bacterial vaginosis			
subjects affected / exposed	1 / 47 (2.13%)	2 / 50 (4.00%)	0 / 47 (0.00%)
occurrences (all)	1	2	0
Cervicitis			
subjects affected / exposed	1 / 47 (2.13%)	2 / 50 (4.00%)	0 / 47 (0.00%)
occurrences (all)	1	2	0
Gastroenteritis			
subjects affected / exposed	1 / 47 (2.13%)	2 / 50 (4.00%)	0 / 47 (0.00%)
occurrences (all)	1	2	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 47 (0.00%)	3 / 50 (6.00%)	0 / 47 (0.00%)
occurrences (all)	0	3	0
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 47 (0.00%)	2 / 50 (4.00%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Candida infection			
subjects affected / exposed	1 / 47 (2.13%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	1	1	0
Vaginitis gardnerella			
subjects affected / exposed	1 / 47 (2.13%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	1	1	0
Escherichia urinary tract infection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Genital candidiasis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0

Pulpitis dental			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Pyuria			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Skin candida			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Ureaplasma infection			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hypernatraemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Iron deficiency			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Atosiban (Fetal)	Retosiban (Neonatal)	Atosiban (Neonatal)
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	6 / 50 (12.00%)	23 / 46 (50.00%)	17 / 50 (34.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Eyelid haemangioma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	0	1
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Pregnancy, puerperium and perinatal conditions			
Foetal hypokinesia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	1	0	0
Oligohydramnios			
subjects affected / exposed	1 / 50 (2.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	1	0	0
Postpartum haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Gestational hypertension			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Polyhydramnios			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Premature labour			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Preterm premature rupture of membranes			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Jaundice neonatal			

subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	2 / 50 (4.00%)
occurrences (all)	0	1	2
Cephalhaematoma			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Suprapubic pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Scrotal oedema			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
Testicular retraction			

subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Breast engorgement			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Uterine atony			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Vulval oedema			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pruritus			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Neonatal respiratory distress syndrome			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Transient tachypnoea of the newborn			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	1 / 50 (2.00%)
occurrences (all)	0	1	1
Apnoea			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	0	1
Choking			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
Respiratory acidosis			

subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	0 / 50 (0.00%) 0
Respiratory disorder neonatal subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	1 / 50 (2.00%) 1
Tachypnoea subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	0 / 50 (0.00%) 0
Use of accessory respiratory muscles subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	1 / 50 (2.00%) 1
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Agitation subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Mood swings subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Investigations			
Escherichia test positive subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Psychiatric evaluation abnormal subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Candida test positive subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Haemoglobin decreased			



subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Klebsiella test positive subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
White blood cell count increased subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Abdominal wound dehiscence subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Congenital, familial and genetic disorders Congenital hydronephrosis subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	0 / 50 (0.00%) 0
Hydrocele subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	1 / 50 (2.00%) 1
Cardiac disorders Foetal heart rate disorder subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 4	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Foetal heart rate deceleration abnormality subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Bradycardia foetal subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Tachycardia subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	0 / 50 (0.00%) 0

Bradycardia subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	1 / 50 (2.00%) 1
Tachycardia foetal subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Nervous system disorders Cerebral haemorrhage subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	0 / 50 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Burning sensation subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Blood and lymphatic system disorders Polycythaemia neonatorum subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	0 / 50 (0.00%) 0
Anaemia subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Anaemia of pregnancy subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Leukocytosis subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Ear and labyrinth disorders			

Auditory disorder subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	1 / 50 (2.00%) 1
Eye disorders Eyelid oedema subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	0 / 50 (0.00%) 0
Gastrointestinal disorders Infantile colic subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	1 / 50 (2.00%) 1
Constipation subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	0 / 50 (0.00%) 0
Flatulence subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	1 / 50 (2.00%) 1
Inguinal hernia subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	1 / 50 (2.00%) 1
Regurgitation subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	1 / 50 (2.00%) 1
Umbilical hernia subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	1 / 50 (2.00%) 1
Vomiting subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	0 / 50 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Abdominal rigidity subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Dental caries			

subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Gingival bleeding subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Toothache subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Hepatobiliary disorders			
Hyperbilirubinaemia neonatal subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	10 / 46 (21.74%) 10	8 / 50 (16.00%) 8
Jaundice subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	2 / 46 (4.35%) 3	0 / 50 (0.00%) 0
Hyperbilirubinaemia subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	1 / 50 (2.00%) 1
Hepatic steatosis subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Skin and subcutaneous tissue disorders			
Acne infantile subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	1 / 50 (2.00%) 1
Blister subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	1 / 50 (2.00%) 1
Dry skin subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	0 / 50 (0.00%) 0
Macule subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Pruritus			

subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Renal and urinary disorders Renal pain subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Arthralgia subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Flank pain subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Neck pain subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Bacterial vaginosis subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Cervicitis subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Gastroenteritis			

subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Vaginitis gardnerella			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Genital candidiasis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Pulpitis dental			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Pyuria			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 46 (0.00%)	2 / 50 (4.00%)
occurrences (all)	0	0	3
Skin candida			

subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Ureaplasma infection subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Vaginal infection subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Metabolism and nutrition disorders			
Hypernatraemia subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	0 / 50 (0.00%) 0
Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Metabolic acidosis subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	1 / 50 (2.00%) 1
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0
Iron deficiency subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 46 (0.00%) 0	0 / 50 (0.00%) 0

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 January 2015	Amendment No. 1 The following changes are reflected in the Country-Specific Protocol Amendment for Applicable Sites in France: Inclusion criteria 1 and 2 were amended to specify that subjects must be at least 18 years of age to participate in Study 200721, and subjects who participate in Study 200721 must also agree to participate in Study 200722, a separate infant follow-up study. Text was revised throughout to reflect the change in the subject age criterion and the requirement to enroll in the infant follow-up study. Section 9.2 was updated to clarify that the study would be conducted using the current version of the Declaration of Helsinki. Finally, an appendix was added that categorizes laboratory samples into those supporting study conduct and those that may be analyzed at a later date.
29 January 2015	Amendment No. 2 The following changes are reflected in the Country-Specific Protocol Amendment for Applicable United Kingdom Sites: The text from Section 5.3 has been clarified. The intent of the language remains the same, but the clarification confirms there is no requirement for the investigator to discuss unblinding with the PPD medical monitor in order to rapidly unblind treatment for a study subject if needed. In addition, Section 9.2 was updated to clarify that the study would be conducted using the current version of the Declaration of Helsinki
04 February 2015	Amendment No. 3 The following changes are reflected in the Country-Specific Protocol Amendment for Applicable Swedish Sites: An appendix was added to list the medications considered strong, moderate, and weak CYP3A4 (cytochrome P450 3A4 enzyme) inhibitors and inducers.
22 August 2016	Amendment No. 4: Clarified the methods for documenting Screening GA. Clarified that co-morbid conditions would exclude a subject with known or suspected maternal Zika infection. Revised guidance regarding adequate treatment response and defined inadequate treatment response. Added procedures to be followed for managing dose interruptions; and allowed pessary use if started before the current episode of preterm labor. Revised the requirements for continuous fetal heart rate monitoring to a minimum of 6 hours from the start of the infusion or from the start of a dose increase, provided the heart rate pattern was consistently reassuring. Clarified that confirmation of uterine contraction eligibility criterion must occur within 60 minutes before study drug dosing. Removed the follow-up amniotic fluid index (AFI) by abdominal ultrasound as a fetal safety endpoint. Removed the requirement for an ultrasound for AFI determination within 12 hours of completion of study treatment. Revised the method used for adjusting multiplicity of the key secondary endpoints from a stepwise Holm's test to a sequential testing method.
21 December 2016	Amendment No. 5: Remove the screening urine drug and alcohol tests. Remove requirement that investigator confirm uterine contraction rate and cervical dilation after randomization and just before study drug administration. Add that after randomization and prior to study drug administration investigators will re-assess that tocolytic therapy is still indicated, according to their medical discretion. Clarify that an abdominal ultrasound to assess fetal growth is needed at Screening or before retreatment unless the most recent ultrasound is within 3 weeks (21 days) before the date of randomization or the date of retreatment. Update the list of maternal drug-related events to clarify the reporting process for events of subsequent preterm labor and hospitalization for delivery that are not worse than expected. Add that the amniotic fluid index should be measured using the 4-quadrant method. Remove changes detailed in the country-specific amendment for sites in France (dated 29 Jan 2015). Incorporate other administrative changes.

Notes:



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## **Interruptions (globally)**

Were there any global interruptions to the trial? No

## **Limitations and caveats**

None reported