Clinical trial results:
A phase 3, double-blind, randomized, placebo-controlled study to assess the safety and efficacy of a single oral administration of nolasiban to improve pregnancy rates following In vitro Fertilization (IVF) or Intra-cytoplasmic Sperm Injection (ICSI) in Day 3 and Day 5 fresh embryo transfer cycles (IMPLANT 2)

Summary

EudraCT number	2016-004266-25
Trial protocol	CZ DE DK BE HU EE ES FI PL
Global end of trial date	19 February 2019

Results information

Result version number	v1 (current)
This version publication date	22 January 2020
First version publication date	22 January 2020

Trial information

Trial identification

Sponsor protocol code	16-OBE001-005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03081208
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ObsEva SA
Sponsor organisation address	12 Chemin des Aulx, Plan-Les-Ouates, Switzerland, 1228
Public contact	Clinical Trial Director, ObsEva S.A., 41 0225523840, clinicaltrials@obseva.ch
Scientific contact	Clinical Trial Director, ObsEva S.A., 41 0225523840, clinicaltrials@obseva.ch

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 January 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to confirm the efficacy of a single oral 900 mg dose of nolasiban to increase the ongoing clinical pregnancy rate at 10 weeks post-embryo transfer (ET) day.

Protection of trial subjects:

This study was to be performed in accordance with the protocol, with the ethical principles that have their origin in the Declaration of Helsinki, with the International Council for Harmonization (ICH) Harmonized Tripartite Guideline for Good Clinical Practice (GCP), with the European Union Clinical Trial Directive, and with all applicable local laws and regulations.

Before initiation of the study at a given site, written approval of the protocol, the Informed Consent Form (ICF), and any information presented to potential subjects had to be obtained from the appropriate Independent Ethics Committee (IEC).

Background therapy:

Subjects in this study were undergoing controlled ovarian hyperstimulation (COH) in preparation for IVF/ICSI according to the clinical center's practice, following a gonadotropin releasing hormone (GnRH) antagonist protocol. Final follicular maturation was to be performed with one administration of human chorionic gonadotropin (hCG), and luteal support was to be provided using vaginal micronized natural P4 at 600 mg daily (or local alternative if not available) starting from the morning after oocyte pick-up (OPU) until at least the Week 6 visit (for subjects with positive pregnancy test at the Week 2 visit).

Evidence for comparator: -

Actual start date of recruitment	08 March 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 217
Country: Number of subjects enrolled	Spain: 52
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Czech Republic: 241
Country: Number of subjects enrolled	Denmark: 43
Country: Number of subjects enrolled	Estonia: 17
Country: Number of subjects enrolled	Finland: 11
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hungary: 176
Worldwide total number of subjects	779
EEA total number of subjects	779

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	779
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient screened: 08Mar2017
Last patient completed: 04Jan2018
Last neonatal follow-up data: 06Sep2018
Last infant follow-up data: 23Jan2019

Study conducted at 43 study sites in 9 countries [Czech Rep (8), Poland (6), Hungary (4), Spain (8), Denmark (4), Belgium (4), Estonia (2), Germany (4) and Finland (3)].

Pre-assignment

Screening details:

A total of 1103 potential subjects were screened, of whom 779 were randomized.
One randomized subject who was randomized to nolasiban in the D5 subgroup was found to be ineligible for the study and did not receive study treatment. Consequently, this subject was not included in the Full Analysis Set (FAS).
Therefore, the FAS included 778 subject.

Period 1

Period 1 title	Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

As soon as the last subject completed the last scheduled visit up to Week 10 and all data up to this visit were entered into the clinical database, cleaned, and locked, the treatment groups were unblinded to the sponsor, and the results up to the Week 10 visit were analyzed and described in a CSR.

However Subjects and investigators remained blinded until the end of the 6-month infant follow-up.

Arms

Are arms mutually exclusive?	Yes
Arm title	nolasiban 900mg (overall Day 3 and Day 5)

Arm description:

A single oral dose of 900 mg nolasiban was administered to the subject at the investigational site about 4 hours prior to the single embryo transfer (SET).

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

Dosage and administration details:

On the day of SET, subjects received a single oral dose of 900 mg nolasiban dispersed in water approximately 4 hours prior to the transfer procedure.

Arm title	placebo (overall Day 3 and Day 5)

Arm description:

A single oral dose of matching placebo was administered to the subject at the investigational site about 4 hours prior to the SET.

Arm type	Placebo

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

On the day of SET, subjects received a single oral dose of matching placebo, dispersed in water approximately 4 hours prior to the transfer procedure.

Number of subjects in period 1[1]	nolasiban 900mg (overall Day 3 and Day 5)	placebo (overall Day 3 and Day 5)
Started	388	390
Week 10	388	390
Completed	388	390

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Subject 110331 was not treated because she did not meet eligibility criterion no. 9.

Period 2

Period 2 title	Follow-up Period 1
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

As soon as the last subject completed Week 10 and the database was locked, the treatment groups were unblinded to the Sponsor.
Subjects and investigators remained blinded until the end of the 6-month infant follow-up period 2

Arms

Are arms mutually exclusive?	Yes
Arm title	Follow-up 1 - nolasiban overall Day 3 and Day 5

Arm description:

All Women Follow-Up (AWFU) Set: All subjects, treated with nolasiban, who took part in the pregnancy outcome follow-up. This was the analysis set for the analysis of pregnancy outcome data.

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

Dosage and administration details:

On the day of SET, subjects received a single oral dose of 900 mg nolasiban dispersed in water approximately 4 hours prior to the transfer procedure.

Arm title	Follow-up 1 - placebo overall Day 3 and Day 5

Arm description:

All Women Follow-Up (AWFU) Set: All subjects, receiving placebo, who took part in the pregnancy outcome follow-up. This was the analysis set for the analysis of pregnancy outcome data.

Note: Subject 120505 (SET D3, was randomized to nolasiban but received placebo. This subject gave birth to 1 live infant.

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

Dosage and administration details:

On the day of SET, subjects received a single oral dose of matching placebo, dispersed in water approximately 4 hours prior to the transfer procedure.

Number of subjects in period 2	Follow-up 1 - nolasiban overall Day 3 and Day 5	Follow-up 1 - placebo overall Day 3 and Day 5
Started	388	390
Completed	137	112
Not completed	251	279
Not pregnant	250	279
Transferred to other arm/group	1	-
Joined	0	1
Transferred in from other group/arm	-	1

Period 3

Period 3 title	Follow-up Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

As soon as the last subject completed Week 10 and the database was locked, the treatment groups were unblinded to the Sponsor.
Subjects and investigators remained blinded until the end of the 6-month infant follow-up period 2.

Arms

Are arms mutually exclusive?	Yes
Arm title	Follow-up 2 - nolasiban overall Day 3 and Day 5

Arm description:

The AI Analysis Set consists of all infants (whose mothers were treated with nolasiban) assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

Arm type	Experimental

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

Dosage and administration details:

On the day of SET, subjects received a single oral dose of 900 mg nolasiban dispersed in water approximately 4 hours prior to the transfer procedure.

Arm title	Follow-up 2 - placebo overall Day 3 and Day 5

Arm description:

The All Infant (AI) Analysis Set consists of all infants (whose mothers received placebo) assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

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

Dosage and administration details:

On the day of SET, subjects received a single oral dose of matching placebo, dispersed in water approximately 4 hours prior to the transfer procedure.

Number of subjects in period 3	Follow-up 2 - nolasiban overall Day 3 and Day 5	Follow-up 2 - placebo overall Day 3 and Day 5
Started	137	112
Completed	136	109
Not completed	6	5
Pregnancy interruption	1	-
In utero death	-	2
spontaneous abortion	2	-
therapeutic abortion	-	1
Lost to follow-up	3	1
Pregnancy termination	-	1
Joined	5	2
twins	5	2

Baseline characteristics

Reporting groups	
Reporting group title	nolasiban 900mg (overall Day 3 and Day 5)
Reporting group description:	
A single oral dose of 900 mg nolasiban was administered to the subject at the investigational site about 4 hours prior to the single embryo transfer (SET).	
Reporting group title	placebo (overall Day 3 and Day 5)
Reporting group description:	
A single oral dose of matching placebo was administered to the subject at the investigational site about 4 hours prior to the SET.	

Reporting group values	nolasiban 900mg (overall Day 3 and Day 5)	placebo (overall Day 3 and Day 5)	Total
Number of subjects	388	390	778
Age categorical Units: Subjects			
Adults (18-64 years)	388	390	778
Not recorded	0	0	0
Age continuous Units: years			
arithmetic mean	31.1	31.4	
standard deviation	± 3.3	± 3.2	-
Gender categorical Units: Subjects			
Female	388	390	778

Subject analysis sets	
Subject analysis set title	Day 3 Single Embryo Transfer nolasiban
Subject analysis set type	Full analysis
Subject analysis set description:	
subjects treated with 900 mg nolasiban 4hr before single embryo transfer (SET) on Day 3	
Subject analysis set title	Day 3 Single Embryo Transfer placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
subjects receiving placebo 4hr before single embryo transfer (SET) on Day 3 .	
Subject analysis set title	Day 5 Single Embryo Transfer nolasiban
Subject analysis set type	Full analysis
Subject analysis set description:	
subjects treated with 900 mg nolasiban 4hr before single embryo transfer (SET) on Day 5	
Subject analysis set title	Day 5 Single Embryo Transfer placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
subjects receiving placebo 4hr before single embryo transfer (SET) on Day 5	
Subject analysis set title	Safety Analysis: Day 3 Single Embryo Transfer placebo
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Analysis Set consists of all randomized subjects who received study medication (analyzed by	

treatment received)

Subject analysis set title	Safety Analysis: Day 3 Single Embryo Transfer nolasiban
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set consists of all randomized subjects who received study medication (analyzed by treatment received)

Subject analysis set title	Safety Analysis: Day 5 Single Embryo Transfer placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set consists of all randomized subjects who received study medication (analyzed by treatment received)

Subject analysis set title	Safety Analysis: Day 5 Single Embryo Transfer nolasiban
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set consists of all randomized subjects who received study medication (analyzed by treatment received)

Subject analysis set title	Safety Analysis: overall Day 3 and Day 5 SET - placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set consists of all randomized subjects who received study medication (analyzed by treatment received)

Subject analysis set title	Safety Analysis: overall Day 3 and Day 5 SET - nolasiban
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set consists of all randomized subjects who received study medication (analyzed by treatment received)

Subject analysis set title	AWFU - Day 3 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Women Follow-up (AWFU) Set consists of all subjects who took part in the pregnancy outcome follow-up, including the 4 subjects who were lost to follow-up.

Subject analysis set title	AWFU - Day 3 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All Women Follow-up (AWFU) Set consists of all subjects who took part in the pregnancy outcome follow-up, including the 4 subjects who were lost to follow-up.

Subject analysis set title	AWFU - Day 5 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Women Follow-up (AWFU) Set consists of all subjects who took part in the pregnancy outcome follow-up, including the 4 subjects who were lost to follow-up.

Subject analysis set title	AWFU - Day 5 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Women Follow-up (AWFU) Set consists of all subjects who took part in the pregnancy outcome follow-up, including the 4 subjects who were lost to follow-up.

Subject analysis set title	AWFU - Overall Day 3 and Day 5 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Women Follow-up (AWFU) Set consists of all subjects who took part in the pregnancy outcome follow-up, including the 4 subjects who were lost to follow-up.

Subject analysis set title	AWFU - Overall Day 3 and Day 5 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Women Follow-Up (AWFU) Set consists of all subjects who took part in the pregnancy outcome

follow-up, including the 4 subjects who were lost to follow-up.

Subject analysis set title	AF - Day 3 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Fetuses (AF) Set consists of all fetuses for whom data from the Pregnancy Outcome and Neonatal Health form were available.

Subject analysis set title	AF - Day 3 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Fetuses (AF) Set consists of all fetuses for whom data from the Pregnancy Outcome and Neonatal Health form were available.

Subject analysis set title	AF - Day 5 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Fetuses (AF) Set consists of all fetuses for whom data from the Pregnancy Outcome and Neonatal Health form were available.

Subject analysis set title	AF - Day 5 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Fetuses (AF) Set consists of all fetuses for whom data from the Pregnancy Outcome and Neonatal Health form were available.

Subject analysis set title	AF - overall Day 3 and Day 5 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Fetuses (AF) Set consists of all fetuses for whom data from the Pregnancy Outcome and Neonatal Health form were available.

Subject analysis set title	AF - overall Day 3 and Day 5 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Fetuses (AF) Set consists of all fetuses for whom data from the Pregnancy Outcome and Neonatal Health form were available.

Subject analysis set title	AI - Day 3 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Infant (AI) Analysis Set consists of all infants assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

Subject analysis set title	AI - Day 3 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Infant (AI) Analysis Set consists of all infants assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

Subject analysis set title	AI - Day 5 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Infant (AI) Analysis Set consists of all infants assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

Subject analysis set title	AI - Day 5 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Infant (AI) Analysis Set consists of all infants assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

Subject analysis set title	AI - overall Day 3 and Day 5 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Infant (AI) Analysis Set consists of all infants assessed at birth and/or at least 28 days post-

delivery and/or who had adverse events recorded.

Subject analysis set title	AI - overall Day 3 and Day 5 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Infant (AI) Analysis Set consists of all infants assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

Subject analysis set title	AIFU - overall Day 3 and Day 5 - nolasiban
Subject analysis set type	Safety analysis

Subject analysis set description:

All infants entered into the 6-month infant follow-up (AIFU) whose mothers received nolasiban on either Day 3 or Day 5 Embryo transfers

Subject analysis set title	AIFU - overall Day 3 and Day 5 - placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

All infants entered into the 6-month infant follow-up (AIFU) whose mothers received placebo on either Day 3 or Day 5 Embryo transfers

Subject analysis set title	AIFU - Day 3 nolasiban
Subject analysis set type	Safety analysis

Subject analysis set description:

All infants entered into the 6-month infant follow-up (AIFU) whose mothers received nolasiban on Day 3 Embryo transfer

Subject analysis set title	AIFU - Day 3 placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

All infants entered into the 6-month infant follow-up (AIFU) whose mothers received placebo on Day 3 Embryo transfer

Subject analysis set title	AIFU - Day 5 nolasiban
Subject analysis set type	Safety analysis

Subject analysis set description:

All infants entered into the 6-month infant follow-up (AIFU) whose mothers received nolasiban on Day 5 Embryo transfer

Subject analysis set title	AIFU - Day 5 placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

All infants entered into the 6-month infant follow-up (AIFU) whose mothers received placebo on Day 5 Embryo transfer

Reporting group values	Day 3 Single Embryo Transfer nolasiban	Day 3 Single Embryo Transfer placebo	Day 5 Single Embryo Transfer nolasiban
Number of subjects	194	194	194
Age categorical			
Units: Subjects			
Adults (18-64 years)	194	194	194
Not recorded	0	0	0
Age continuous			
Units: years			
arithmetic mean	31.1	31.4	31.1
standard deviation	± 3.2	± 3.3	± 3.3
Gender categorical			
Units: Subjects			
Female	194	194	194

Reporting group values	Day 5 Single Embryo Transfer	Safety Analysis: Day 3 Single Embryo	Safety Analysis: Day 3 Single Embryo

	placebo	Transfer placebo	Transfer nolasiban
Number of subjects	196	195	193
Age categorical Units: Subjects			
Adults (18-64 years)	196		
Not recorded	0		
Age continuous Units: years			
arithmetic mean	31.3		
standard deviation	± 3.2	±	±
Gender categorical Units: Subjects			
Female	196		

Reporting group values	Safety Analysis: Day 5 Single Embryo Transfer placebo	Safety Analysis: Day 5 Single Embryo Transfer nolasiban	Safety Analysis: overall Day 3 and Day 5 SET - placebo
Number of subjects	196	194	391
Age categorical Units: Subjects			
Adults (18-64 years)			
Not recorded			
Age continuous Units: years			
arithmetic mean			
standard deviation	±	±	±
Gender categorical Units: Subjects			
Female			

Reporting group values	Safety Analysis: overall Day 3 and Day 5 SET - nolasiban	AWFU - Day 3 SET placebo	AWFU - Day 3 SET nolasiban
Number of subjects	387	44	48
Age categorical Units: Subjects			
Adults (18-64 years)			
Not recorded			
Age continuous Units: years			
arithmetic mean		31.2	31.1
standard deviation	±	± 3.1	± 3.5
Gender categorical Units: Subjects			
Female			

Reporting group values	AWFU - Day 5 SET placebo	AWFU - Day 5 SET nolasiban	AWFU - Overall Day 3 and Day 5 SET placebo
Number of subjects	68	89	112

Age categorical Units: Subjects			
Adults (18-64 years) Not recorded			
Age continuous Units: years arithmetic mean standard deviation	 31.5 ± 3.4	 31.1 ± 3.3	 31.4 ± 3.3
Gender categorical Units: Subjects			
Female			

Reporting group values	AWFU - Overall Day 3 and Day 5 SET nolasiban	AF - Day 3 SET placebo	AF - Day 3 SET nolasiban
Number of subjects	137	44	44
Age categorical Units: Subjects			
Adults (18-64 years) Not recorded			
Age continuous Units: years arithmetic mean standard deviation	 31.1 ± 3.3	 ±	 ±
Gender categorical Units: Subjects			
Female			

Reporting group values	AF - Day 5 SET placebo	AF - Day 5 SET nolasiban	AF - overall Day 3 and Day 5 SET placebo
Number of subjects	66	92	110
Age categorical Units: Subjects			
Adults (18-64 years) Not recorded			
Age continuous Units: years arithmetic mean standard deviation	 ±	 ±	 ±
Gender categorical Units: Subjects			
Female			

Reporting group values	AF - overall Day 3 and Day 5 SET nolasiban	AI - Day 3 SET placebo	AI - Day 3 SET nolasiban
Number of subjects	136	43	44
Age categorical Units: Subjects			
Adults (18-64 years) Not recorded			

Age continuous Units: years arithmetic mean standard deviation	±	±	±
Gender categorical Units: Subjects			
Female			

Reporting group values	AI - Day 5 SET placebo	AI - Day 5 SET nolasiban	AI - overall Day 3 and Day 5 SET placebo
Number of subjects	66	92	109
Age categorical Units: Subjects			
Adults (18-64 years) Not recorded			
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Gender categorical Units: Subjects			
Female			

Reporting group values	AI - overall Day 3 and Day 5 SET nolasiban	AIFU - overall Day 3 and Day 5 - nolasiban	AIFU - overall Day 3 and Day 5 - placebo
Number of subjects	136	124	99
Age categorical Units: Subjects			
Adults (18-64 years) Not recorded			
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Gender categorical Units: Subjects			
Female			

Reporting group values	AIFU - Day 3 nolasiban	AIFU - Day 3 placebo	AIFU - Day 5 nolasiban
Number of subjects	43	40	81
Age categorical Units: Subjects			
Adults (18-64 years) Not recorded			
Age continuous Units: years arithmetic mean standard deviation	±	±	±

Gender categorical Units: Subjects			
Female			

Reporting group values	AIFU - Day 5 placebo		
Number of subjects	59		
Age categorical Units: Subjects			
Adults (18-64 years) Not recorded			
Age continuous Units: years arithmetic mean standard deviation	 ±		
Gender categorical Units: Subjects			
Female			

End points

End points reporting groups

Reporting group title	nolasiban 900mg (overall Day 3 and Day 5)
Reporting group description:	
A single oral dose of 900 mg nolasiban was administered to the subject at the investigational site about 4 hours prior to the single embryo transfer (SET).	
Reporting group title	placebo (overall Day 3 and Day 5)
Reporting group description:	
A single oral dose of matching placebo was administered to the subject at the investigational site about 4 hours prior to the SET.	
Reporting group title	Follow-up 1 - nolasiban overall Day 3 and Day 5
Reporting group description:	
All Women Follow-Up (AWFU) Set: All subjects, treated with nolasiban, who took part in the pregnancy outcome follow-up. This was the analysis set for the analysis of pregnancy outcome data.	
Reporting group title	Follow-up 1 - placebo overall Day 3 and Day 5
Reporting group description:	
All Women Follow-Up (AWFU) Set: All subjects, receiving placebo, who took part in the pregnancy outcome follow-up. This was the analysis set for the analysis of pregnancy outcome data. Note: Subject 120505 (SET D3, was randomized to nolasiban but received placebo. This subject gave birth to 1 live infant.	
Reporting group title	Follow-up 2 - nolasiban overall Day 3 and Day 5
Reporting group description:	
The AI Analysis Set consists of all infants (whose mothers were treated with nolasiban) assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.	
Reporting group title	Follow-up 2 - placebo overall Day 3 and Day 5
Reporting group description:	
The All Infant (AI) Analysis Set consists of all infants (whose mothers received placebo) assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.	
Subject analysis set title	Day 3 Single Embryo Transfer nolasiban
Subject analysis set type	Full analysis
Subject analysis set description:	
subjects treated with 900 mg nolasiban 4hr before single embryo transfer (SET) on Day 3	
Subject analysis set title	Day 3 Single Embryo Transfer placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
subjects receiving placebo 4hr before single embryo transfer (SET) on Day 3 .	
Subject analysis set title	Day 5 Single Embryo Transfer nolasiban
Subject analysis set type	Full analysis
Subject analysis set description:	
subjects treated with 900 mg nolasiban 4hr before single embryo transfer (SET) on Day 5	
Subject analysis set title	Day 5 Single Embryo Transfer placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
subjects receiving placebo 4hr before single embryo transfer (SET) on Day 5	
Subject analysis set title	Safety Analysis: Day 3 Single Embryo Transfer placebo
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Analysis Set consists of all randomized subjects who received study medication (analyzed by treatment received)	
Subject analysis set title	Safety Analysis: Day 3 Single Embryo Transfer nolasiban
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set consists of all randomized subjects who received study medication (analyzed by treatment received)

Subject analysis set title	Safety Analysis: Day 5 Single Embryo Transfer placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set consists of all randomized subjects who received study medication (analyzed by treatment received)

Subject analysis set title	Safety Analysis: Day 5 Single Embryo Transfer nolasiban
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set consists of all randomized subjects who received study medication (analyzed by treatment received)

Subject analysis set title	Safety Analysis: overall Day 3 and Day 5 SET - placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set consists of all randomized subjects who received study medication (analyzed by treatment received)

Subject analysis set title	Safety Analysis: overall Day 3 and Day 5 SET - nolasiban
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set consists of all randomized subjects who received study medication (analyzed by treatment received)

Subject analysis set title	AWFU - Day 3 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Women Follow-up (AWFU) Set consists of all subjects who took part in the pregnancy outcome follow-up, including the 4 subjects who were lost to follow-up.

Subject analysis set title	AWFU - Day 3 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All Women Follow-up (AWFU) Set consists of all subjects who took part in the pregnancy outcome follow-up, including the 4 subjects who were lost to follow-up.

Subject analysis set title	AWFU - Day 5 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Women Follow-up (AWFU) Set consists of all subjects who took part in the pregnancy outcome follow-up, including the 4 subjects who were lost to follow-up.

Subject analysis set title	AWFU - Day 5 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Women Follow-up (AWFU) Set consists of all subjects who took part in the pregnancy outcome follow-up, including the 4 subjects who were lost to follow-up.

Subject analysis set title	AWFU - Overall Day 3 and Day 5 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Women Follow-up (AWFU) Set consists of all subjects who took part in the pregnancy outcome follow-up, including the 4 subjects who were lost to follow-up.

Subject analysis set title	AWFU - Overall Day 3 and Day 5 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Women Follow-Up (AWFU) Set consists of all subjects who took part in the pregnancy outcome follow-up, including the 4 subjects who were lost to follow-up.

Subject analysis set title	AF - Day 3 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Fetuses (AF) Set consists of all fetuses for whom data from the Pregnancy Outcome and Neonatal Health form were available.

Subject analysis set title	AF - Day 3 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Fetuses (AF) Set consists of all fetuses for whom data from the Pregnancy Outcome and Neonatal Health form were available.

Subject analysis set title	AF - Day 5 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Fetuses (AF) Set consists of all fetuses for whom data from the Pregnancy Outcome and Neonatal Health form were available.

Subject analysis set title	AF - Day 5 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Fetuses (AF) Set consists of all fetuses for whom data from the Pregnancy Outcome and Neonatal Health form were available.

Subject analysis set title	AF - overall Day 3 and Day 5 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Fetuses (AF) Set consists of all fetuses for whom data from the Pregnancy Outcome and Neonatal Health form were available.

Subject analysis set title	AF - overall Day 3 and Day 5 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Fetuses (AF) Set consists of all fetuses for whom data from the Pregnancy Outcome and Neonatal Health form were available.

Subject analysis set title	AI - Day 3 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Infant (AI) Analysis Set consists of all infants assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

Subject analysis set title	AI - Day 3 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Infant (AI) Analysis Set consists of all infants assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

Subject analysis set title	AI - Day 5 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Infant (AI) Analysis Set consists of all infants assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

Subject analysis set title	AI - Day 5 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Infant (AI) Analysis Set consists of all infants assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

Subject analysis set title	AI - overall Day 3 and Day 5 SET placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Infant (AI) Analysis Set consists of all infants assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

Subject analysis set title	AI - overall Day 3 and Day 5 SET nolasiban
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The All Infant (AI) Analysis Set consists of all infants assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

Subject analysis set title	AIFU - overall Day 3 and Day 5 - nolasiban
Subject analysis set type	Safety analysis

Subject analysis set description:

All infants entered into the 6-month infant follow-up (AIFU) whose mothers received nolasiban on either Day 3 or Day 5 Embryo transfers

Subject analysis set title	AIFU - overall Day 3 and Day 5 - placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

All infants entered into the 6-month infant follow-up (AIFU) whose mothers received placebo on either Day 3 or Day 5 Embryo transfers

Subject analysis set title	AIFU - Day 3 nolasiban
Subject analysis set type	Safety analysis

Subject analysis set description:

All infants entered into the 6-month infant follow-up (AIFU) whose mothers received nolasiban on Day 3 Embryo transfer

Subject analysis set title	AIFU - Day 3 placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

All infants entered into the 6-month infant follow-up (AIFU) whose mothers received placebo on Day 3 Embryo transfer

Subject analysis set title	AIFU - Day 5 nolasiban
Subject analysis set type	Safety analysis

Subject analysis set description:

All infants entered into the 6-month infant follow-up (AIFU) whose mothers received nolasiban on Day 5 Embryo transfer

Subject analysis set title	AIFU - Day 5 placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

All infants entered into the 6-month infant follow-up (AIFU) whose mothers received placebo on Day 5 Embryo transfer

Primary: Number of women pregnant at 10 weeks post-SET

End point title	Number of women pregnant at 10 weeks post-SET

End point description:

End point type	Primary

End point timeframe:

10 weeks after embryo transfer

End point values	nolasiban 900mg (overall Day 3 and Day 5)	placebo (overall Day 3 and Day 5)	Day 3 Single Embryo Transfer nolasiban	Day 3 Single Embryo Transfer placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	388	390	194	194
Units: number of pregnant women				
pregnant at week 10	138	111	49	43
not pregnant at week 10	250	279	145	151

End point values	Day 5 Single Embryo Transfer nolasiban	Day 5 Single Embryo Transfer placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	194	196		
Units: number of pregnant women				
pregnant at week 10	89	68		
not pregnant at week 10	105	128		

Statistical analyses

Statistical analysis title	OPR 10 Weeks Post-SET – Overall D3/D5: Main Model
Statistical analysis description:	
Ongoing Pregnancy Rate 10 Weeks Post-SET – Overall D3/D5: Main Model (FAS)	
Comparison groups	nolasiban 900mg (overall Day 3 and Day 5) v placebo (overall Day 3 and Day 5)
Number of subjects included in analysis	778
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.031 [2]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	1.99

Notes:

[1] - The primary analysis of the primary efficacy endpoint was performed on the overall D3/D5 FAS by fitting an exact logistic regression model with treatment as the independent variable, the day of transfer (SET D3 or SET D5) as a covariate, and the clinical site as a stratum.

[2] - p-value calculated based on exact conditional distribution.

Statistical analysis title	OPR 10 Weeks Post-SET Day 3
Statistical analysis description:	
Ongoing Pregnancy Rate 10 Weeks Post-SET Day 3 of Embryo Transfer Using the Main Model (FAS)	
Comparison groups	Day 3 Single Embryo Transfer nolasiban v Day 3 Single Embryo Transfer placebo
Number of subjects included in analysis	388
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.477 [4]
Method	Regression, Linear
Parameter estimate	Odds ratio (OR)
Point estimate	1.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.96

Notes:

[3] - Odds ratio and 95% CI estimated using a stratified exact logistic regression model with fixed effect for treatment group and site as a stratification factor.
[4] - p-value calculated based on exact conditional distribution.

Statistical analysis title	OPR 10 Weeks Post-SET Day 5

Statistical analysis description:

Ongoing Pregnancy Rate 10 Weeks Post-SET on Day 5 Embryo of Transfer Using the Main Model (FAS)

Comparison groups	Day 5 Single Embryo Transfer nolasiban v Day 5 Single Embryo Transfer placebo
Number of subjects included in analysis	390
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.034 [6]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	2.47

Notes:

[5] - Odds ratio and 95% CI estimated using a stratified exact logistic regression model with fixed effect for treatment group and site as a stratification factor.
[6] - p-value calculated based on exact conditional distribution.

Primary: Percentage of women pregnant at week 10 post-SET

End point title	Percentage of women pregnant at week 10 post-SET

End point description:

Intra-uterine pregnancy with fetal heartbeat at 10 weeks post-SET day.

End point type	Primary

End point timeframe:

Pregnant 10 weeks after single embryo transfer (SET)

End point values	nolasiban 900mg (overall Day 3 and Day 5)	placebo (overall Day 3 and Day 5)	Day 3 Single Embryo Transfer nolasiban	Day 3 Single Embryo Transfer placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	388	390	194[7]	194[8]
Units: percent				
number (not applicable)	35.6	28.5	25.3	22.2

Notes:

[7] - for statistical values see previous table for Day 3 ET

[8] - for statistical values see previous table for Day 3 ET

End point values	Day 5 Single Embryo Transfer nolasiban	Day 5 Single Embryo Transfer placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	194[9]	196[10]		
Units: percent				
number (not applicable)	45.9	34.7		

Notes:

[9] - for statistical values see previous table for Day 5 ET

[10] - for statistical values see previous table for Day 5 ET

Statistical analyses

Statistical analysis title	% OPR 10 Weeks Post-SET Day 3
Comparison groups	Day 3 Single Embryo Transfer nolasiban v Day 3 Single Embryo Transfer placebo
Number of subjects included in analysis	388
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	= 0.477
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.96

Notes:

[11] - Separate exact logistic regression models for the SET D3 and the SET D5 transfer groups were also performed. The ongoing pregnancy rate 10 weeks post-SET by day of transfer is presented for the FAS.
This analysis uses a similar stratified exact logistic regression analysis except that day is no longer a covariate since SET D3 and SET D5 are analyzed separately.

Statistical analysis title	% OPR 10 Weeks Post-SET Day 5

Statistical analysis description:

Separate exact logistic regression models for the SET D3 and the SET D5 transfer groups were also performed. The ongoing pregnancy rate 10 weeks post-SET by day of transfer is presented for the FAS. This analysis uses a similar stratified exact logistic regression analysis except that day is no longer a covariate since SET D3 and SET D5 are analyzed separately.

Comparison groups	Day 5 Single Embryo Transfer nolasiban v Day 5 Single Embryo Transfer placebo
Number of subjects included in analysis	390
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.034
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.59

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	2.47

Secondary: Number of Live births after 24 weeks of gestation

End point title	Number of Live births after 24 weeks of gestation

End point description:

All subjects who took part in the pregnancy outcome follow-up, analyzed according to treatment received (used for the analysis of pregnancy outcome data for the subjects).

End point type	Secondary

End point timeframe:

After 24 weeks of gestation

End point values	nolasiban 900mg (overall Day 3 and Day 5)	placebo (overall Day 3 and Day 5)	Day 3 Single Embryo Transfer nolasiban	Day 3 Single Embryo Transfer placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	388	390	194	194
Units: Number of live births				
Live Birth Rate - YES	135	108	48	43
Live birth Rate - NO	253	282	146	151

End point values	Day 5 Single Embryo Transfer nolasiban	Day 5 Single Embryo Transfer placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	194	196		
Units: Number of live births				
Live Birth Rate - YES	87	65		
Live birth Rate - NO	107	131		

Statistical analyses

Statistical analysis title	Live Birth Rate - Overall D3/D5

Statistical analysis description:

Key Secondary Efficacy Endpoint: Live Birth Rate – Loss to Follow- Up Assigned as a Positive Response (FAS).

(Results assuming a negative response in case of loss to follow-up were consistent with those assuming a positive
response in case of loss to follow-up.

A total of 4 subjects were lost to follow-up, 1 in the placebo group and 3 in the nolasiban group; consequently, differences between the analyses using different imputation methods for these subjects were minimal)

Comparison groups	nolasiban 900mg (overall Day 3 and Day 5) v placebo (overall Day 3 and Day 5)
Number of subjects included in analysis	778
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	= 0.025 [13]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	2

Notes:

[12] - The key secondary efficacy endpoint was performed on the overall D3/D5 FAS by fitting an exact logistic regression model with treatment as the independent variable, the day of transfer (SET D3 or SET D5) as a covariate, and the clinical site as a stratum.
[13] - p-value calculated based on exact conditional distribution.

Statistical analysis title	Live Birth Rate - D3 only

Statistical analysis description:

Day 3 only Embryo transfer

Comparison groups	Day 3 Single Embryo Transfer nolasiban v Day 3 Single Embryo Transfer placebo
Number of subjects included in analysis	388
Analysis specification	Pre-specified
Analysis type	other[14]
P-value	= 0.552 [15]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.91

Notes:

[14] - Odds ratio and 95% CI estimated using logistic regression model with fixed effects for treatment group and site as a
stratification factor.
[15] - p-value calculated based on exact conditional distribution.

Statistical analysis title	Live Birth Rate - D5 only
Comparison groups	Day 5 Single Embryo Transfer nolasiban v Day 5 Single Embryo Transfer placebo

Number of subjects included in analysis	390
Analysis specification	Pre-specified
Analysis type	other[16]
P-value	= 0.025 [17]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	2.56

Notes:

[16] - Day 5 only embryo transfer

[17] - p-value calculated based on exact conditional distribution.

Secondary: Percentage of Live Birth after 24 weeks gestation

End point title	Percentage of Live Birth after 24 weeks gestation

End point description:

End point type	Secondary

End point timeframe:

After 24 weeks gestation

End point values	nolasiban 900mg (overall Day 3 and Day 5)	placebo (overall Day 3 and Day 5)	Day 3 Single Embryo Transfer nolasiban	Day 3 Single Embryo Transfer placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	388	390	194[18]	194[19]
Units: Percentage of live birth				
number (not applicable)				
Live Birth Rate -YES	34.8	27.7	24.7	22.2
Live Birth Rate - NO	65.2	72.3	75.3	77.8

Notes:

[18] - for statistical values see previous table for Day 3 ET

[19] - for statistical values see previous table for Day 3 ET

End point values	Day 5 Single Embryo Transfer nolasiban	Day 5 Single Embryo Transfer placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	194[20]	196[21]		
Units: Percentage of live birth				
number (not applicable)				
Live Birth Rate -YES	44.8	33.2		
Live Birth Rate - NO	55.2	66.8		

Notes:

[20] - for statistical values see previous table for Day 5 ET

[21] - for statistical values see previous table for Day 5 ET

Statistical analyses

No statistical analyses for this end point

Secondary: Miscarriage Rate between Week 10 and Week 24 gestation

End point title	Miscarriage Rate between Week 10 and Week 24 gestation

End point description:

A miscarriage was defined as any pregnancy loss prior to 24 weeks.

In the overall D3/D5 group and the SET D5 subgroup, rates of miscarriage between Week 2 and Week 24 were numerically lower for nolasiban than for placebo (23% vs. 30% and 18% vs. 28% respectively); treatment difference was less evident in the SET D3 subgroup (30% for nolasiban vs. 34% for placebo).

End point type	Secondary

End point timeframe:

Miscarriages reported in this table are those occurring post-Week 10 database lock.

End point values	nolasiban 900mg (overall Day 3 and Day 5)	placebo (overall Day 3 and Day 5)	Day 3 Single Embryo Transfer nolasiban	Day 3 Single Embryo Transfer placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	388[22]	390[23]	194	194
Units: Number of miscarriages				
No. of Subjects pregnant at Wk 2	175	155	69	65
Miscarriages between W10 and W24 - YES	3	3	1	0
Miscarriages between W10 and W24 - NO	172	152	68	65
Total Miscarriages from W2 to W24 - YES	40	47	21	22
Total Miscarriages from W2 to W24 - NO	135	108	48	43

Notes:

[22] - For miscarriage rates, the denominator is the number of subjects deemed pregnant at 14 days

[23] - For miscarriage rates, the denominator is the number of subjects deemed pregnant at 14 days

End point values	Day 5 Single Embryo Transfer nolasiban	Day 5 Single Embryo Transfer placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	194	196		
Units: Number of miscarriages				
No. of Subjects pregnant at Wk 2	106	90		
Miscarriages between W10 and W24 - YES	2	3		

Miscarriages between W10 and W24 - NO	104	87		
Total Miscarriages from W2 to W24 - YES	19	25		
Total Miscarriages from W2 to W24 - NO	87	65		

Statistical analyses

No statistical analyses for this end point

Secondary: Neonatal outcomes - AI Set

End point title	Neonatal outcomes - AI Set

End point description:

Analysis of neonatal health data:
Overall, 116 (47%) infants were male and 129 (53%) were female (nolasiban: 67 [49%] and 69 [51%]; placebo: 49 [45%] and 60 [55%]).
Mean (standard deviation [SD]) gestational age at birth: 38.20 (2.82) wks in nolasiban group and 38.75 (1.92) wks in placebo group.
At delivery, mean (SD) weight: 3136.9 (689.7) g in nolasiban group and 3173.9 (517.2) g in placebo group; mean (SD) height: 50.44 (4.55) cm in nolasiban group and 50.88 (3.74) cm in placebo group; and mean (SD) head circumference: 33.70 (2.19) cm in nolasiban group and 34.29 (1.56) cm in placebo group. Mean (SD) Apgar scores: 9.01 (1.50) in nolasiban group and 9.09 (1.28) in placebo group at 1 min, and 9.61 (0.84) and 9.65 (0.76) respectively at 5 mins. Congenital anomalies were present at birth in 5 (4%) infants in nolasiban group and in 4 (4%) in placebo group. Neonatal illnesses were present in 14 (10%) infants in nolasiban group compared to 26 (24%) in placebo

End point type	Secondary

End point timeframe:

All Infants (AI) Set: AIs assessed at birth and/or at least 28 days post-delivery and/or who had AEs recorded.

End point values	Follow-up 1 - nolasiban overall Day 3 and Day 5	Follow-up 1 - placebo overall Day 3 and Day 5		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	109		
Units: Number of infants				
Sex - Male	67	49		
Sex - Female	69	60		
Congenital anomaly (at delivery)	5	4		
Neonatal illness (at delivery)	14	26		
Breastfeeding (at least 28 days after delivery)	111	91		
Admission to intensive care at least 28d post-del	9	9		
neonatal morbidities - at least 28d post-del	26	29		
jaundice	18	20		
respiratory distress syndrome	8	10		
difficulty in breathing	11	2		
difficulty in thermoregulation	6	0		
bronchopulmonary dysplasia	3	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Ages and Stages Questionnaires (ASQ-3) Abnormal Scores

End point title	Ages and Stages Questionnaires (ASQ-3) Abnormal Scores

End point description:

Subjects were invited to complete the Ages and Stages Questionnaire-3 (ASQ-3) at 6 months after birth, corrected for gestational age at birth (i.e., at 6 months after the expected term date).

Abnormal scores were defined in the ASQ-3 User Guide as domain scores below the following cut-offs:
29.65 points for communication,
25.14 points for fine motor,
22.25 points for gross motor,
25.34 points for personal-social, and
27.72 points for problem-solving.

End point type	Other pre-specified

End point timeframe:

To evaluate infant development outcomes 6 months after birth

End point values	AIFU - overall Day 3 and Day 5 - nolasiban	AIFU - overall Day 3 and Day 5 - placebo	AIFU - Day 3 nolasiban	AIFU - Day 3 placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	103[24]	88[25]	38	35[26]
Units: Number of infants below the cut-off				
Communication	2	0	1	0
Fine Motor	19	18	7	8
Gross Motor	21	20	10	8
Personal-Social	17	9	5	4
Problem-Solving	12	3	1	2
Overall	43	33	14	13

Notes:

[24] - 101 subjects for Personal-Social

[25] - 87 subjects: Communication + Gross Motor
86 subjects: Problem-Solving
85 subjects: Fine Motor

[26] - 34 subjects: Communication
33 subjects: Problem-Solving

End point values	AIFU - Day 5 nolasiban	AIFU - Day 5 placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	65[27]	53[28]		
Units: Number of infants below the cut-				

off				
Communication	1	0		
Fine Motor	12	10		
Gross Motor	11	12		
Personal-Social	12	5		
Problem-Solving	11	1		
Overall	29	20		

Notes:

[27] - 63 subjects: Personal-Social

[28] - 52 subjects: Gross Motor
50 subjects: Fine Motor

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TEAEs occurring in subjects or fetuses from the day of study drug administration until 28 days after delivery

Adverse event reporting additional description:

AEs were collected up to 4 wks after last visit date or after date of discontinuation. SAEs in relation to pregnancy + birth were reported until end of study. In case of early study discontinuation, any SAEs were reported up to 4 wks post-treatment admin or up to last study visit, should discontinuation occur after 4 wk post-treatment period

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	nolasiban 900mg (overall Day 3 and Day 5)

Reporting group description:

A single oral dose of 900 mg nolasiban was administered to the subject at the investigational site about 4 hours prior to the single embryo transfer (SET).

Reporting group title	placebo (overall Day 3 and Day 5)

Reporting group description:

A single oral dose of matching placebo was administered to the subject at the investigational site about 4 hours prior to the SET.

Reporting group title	SET Day 5 - nolasiban

Reporting group description: -

Reporting group title	SET Day 5 - placebo

Reporting group description: -

Reporting group title	SET Day 3 - nolasiban

Reporting group description: -

Reporting group title	SET Day 3 - placebo

Reporting group description: -

Reporting group title	All Women Follow-up Set - overall Day 3 and Day 5 - nolasiban

Reporting group description:

AWFU Set consists of all subjects who took part in the pregnancy outcome follow-up, including the 4 subjects who were lost to follow-up

Reporting group title	All Women Follow-up Set - overall Day 3 and Day 5 - placebo

Reporting group description:

AWFU Set consists of all subjects who took part in the pregnancy outcome follow-up, including the 4 subjects who were lost to follow-up

Reporting group title	All infant set - overall Day 3 and Day 5 - nolasiban

Reporting group description:

The All Infant (AI) Analysis Set consists of all infants assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

Reporting group title	All infant set - overall Day 3 and Day 5 - placebo

Reporting group description:

The All Infant (AI) Analysis Set consists of all infants assessed at birth and/or at least 28 days post-delivery and/or who had adverse events recorded.

Serious adverse events	nolasiban 900mg (overall Day 3 and Day 5)	placebo (overall Day 3 and Day 5)	SET Day 5 - nolasiban
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 387 (1.03%)	9 / 391 (2.30%)	2 / 194 (1.03%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Anaesthetic complication pulmonary			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (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
Congenital, familial and genetic disorders			
Trisomy 13			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Turner's syndrome			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (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
Foetal growth restriction			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (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
Atrioventricular septal defect			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (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
Choledochal cyst			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (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 foot malformation			

subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (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 genital malformation female			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (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
Cryptorchism			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (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
Heart disease congenital			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (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
Polydactyly			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal aplasia			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (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 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			

Ectopic pregnancy			
subjects affected / exposed	1 / 387 (0.26%)	4 / 391 (1.02%)	0 / 194 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion spontaneous			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian hyperstimulation syndrome			
subjects affected / exposed	2 / 387 (0.52%)	0 / 391 (0.00%)	2 / 194 (1.03%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adnexal torsion			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (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
Uterine malposition			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (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 lower			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (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 ileus			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (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			
Appendicitis			

subjects affected / exposed	0 / 387 (0.00%)	2 / 391 (0.51%)	0 / 194 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (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
Pneumonia			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	SET Day 5 - placebo	SET Day 3 - nolasiban	SET Day 3 - placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 196 (3.57%)	2 / 193 (1.04%)	2 / 195 (1.03%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Anaesthetic complication pulmonary			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (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			
Trisomy 13			
subjects affected / exposed	0 / 196 (0.00%)	1 / 193 (0.52%)	0 / 195 (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
Turner's syndrome			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal growth restriction			

subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (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
Atrioventricular septal defect			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (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
Choledochal cyst			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (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 foot malformation			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (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 genital malformation female			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (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
Cryptorchism			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (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
Heart disease congenital			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (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
Polydactyly			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal aplasia			

subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (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 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	3 / 196 (1.53%)	1 / 193 (0.52%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion spontaneous			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian hyperstimulation syndrome			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (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
Adnexal torsion			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (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
Uterine malposition			

subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (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
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (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
Meconium ileus			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (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			
Appendicitis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (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
Pneumonia			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	All Women Follow-up Set - overall Day 3 and Day 5 - nolasiban	All Women Follow-up Set - overall Day 3 and Day 5 - placebo	All infant set - overall Day 3 and Day 5 - nolasiban
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 137 (3.65%)	5 / 112 (4.46%)	6 / 136 (4.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Anaesthetic complication pulmonary			

subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (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			
Trisomy 13			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Turner's syndrome			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (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
Foetal growth restriction			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (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
Atrioventricular septal defect			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Choledochal cyst			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital foot malformation			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (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 genital malformation female			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (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
Cryptorchism			

subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (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
Heart disease congenital			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polydactyly			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal aplasia			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular septal defect			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion spontaneous			
subjects affected / exposed	2 / 137 (1.46%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Reproductive system and breast disorders			
Ovarian hyperstimulation syndrome			
subjects affected / exposed	2 / 137 (1.46%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adnexal torsion			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine malposition			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (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 lower			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (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 ileus			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	1 / 136 (0.74%)
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			
Appendicitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (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
Bronchiolitis			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (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
Pneumonia			

subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	All infant set - overall Day 3 and Day 5 - placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 109 (4.59%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Anaesthetic complication pulmonary			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Trisomy 13			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Turner's syndrome			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Foetal growth restriction			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrioventricular septal defect			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Choledochal cyst			

subjects affected / exposed	0 / 109 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Congenital foot malformation				
subjects affected / exposed	1 / 109 (0.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Congenital genital malformation female				
subjects affected / exposed	1 / 109 (0.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cryptorchism				
subjects affected / exposed	1 / 109 (0.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Heart disease congenital				
subjects affected / exposed	0 / 109 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Polydactyly				
subjects affected / exposed	1 / 109 (0.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal aplasia				
subjects affected / exposed	0 / 109 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ventricular septal defect				
subjects affected / exposed	0 / 109 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Abortion induced				

subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abortion spontaneous			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian hyperstimulation syndrome			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adnexal torsion			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine malposition			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meconium ileus			

subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchiolitis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	nolasiban 900mg (overall Day 3 and Day 5)	placebo (overall Day 3 and Day 5)	SET Day 5 - nolasiban
Total subjects affected by non-serious adverse events			
subjects affected / exposed	97 / 387 (25.06%)	101 / 391 (25.83%)	61 / 194 (31.44%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	2	0
Vasodilatation			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	1	0	0
Extremity necrosis			

subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Oocyte harvest			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Cervix cerclage procedure			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	1	0	0
Abortion induced			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	1	0	0
Pregnancy, puerperium and perinatal conditions			
Biochemical pregnancy			
subjects affected / exposed	13 / 387 (3.36%)	21 / 391 (5.37%)	5 / 194 (2.58%)
occurrences (all)	13	21	5
Abortion missed			
subjects affected / exposed	19 / 387 (4.91%)	9 / 391 (2.30%)	11 / 194 (5.67%)
occurrences (all)	19	9	11
Abortion spontaneous			
subjects affected / exposed	6 / 387 (1.55%)	14 / 391 (3.58%)	1 / 194 (0.52%)
occurrences (all)	6	14	1
Haemorrhage in pregnancy			
subjects affected / exposed	4 / 387 (1.03%)	5 / 391 (1.28%)	3 / 194 (1.55%)
occurrences (all)	5	5	3
Abortion threatened			
subjects affected / exposed	1 / 387 (0.26%)	1 / 391 (0.26%)	1 / 194 (0.52%)
occurrences (all)	1	1	1
Blighted ovum			
subjects affected / exposed	1 / 387 (0.26%)	1 / 391 (0.26%)	1 / 194 (0.52%)
occurrences (all)	1	1	1
Abortion incomplete			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Imminent abortion			

subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Subchorionic haematoma			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	2	0
Vomiting in pregnancy			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Foetal growth restriction			
subjects affected / exposed	2 / 387 (0.52%)	0 / 391 (0.00%)	2 / 194 (1.03%)
occurrences (all)	2	0	2
Placenta praevia			
subjects affected / exposed	5 / 387 (1.29%)	2 / 391 (0.51%)	4 / 194 (2.06%)
occurrences (all)	5	2	4
Polyhydramnios			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Cervical incompetence			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Premature separation of placenta			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Threatened labour			
subjects affected / exposed	1 / 387 (0.26%)	2 / 391 (0.51%)	1 / 194 (0.52%)
occurrences (all)	1	2	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Feeling hot			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	1	0	0
Pain			

subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	9 / 387 (2.33%)	12 / 391 (3.07%)	7 / 194 (3.61%)
occurrences (all)	9	17	7
Ovarian hyperstimulation syndrome			
subjects affected / exposed	2 / 387 (0.52%)	4 / 391 (1.02%)	1 / 194 (0.52%)
occurrences (all)	4	4	2
Pelvic pain			
subjects affected / exposed	4 / 387 (1.03%)	4 / 391 (1.02%)	2 / 194 (1.03%)
occurrences (all)	5	5	2
Uterine pain			
subjects affected / exposed	2 / 387 (0.52%)	4 / 391 (1.02%)	1 / 194 (0.52%)
occurrences (all)	2	4	1
Dysmenorrhoea			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Dyspareunia			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Haematosalpinx			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Uterine haematoma			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Uterine haemorrhage			
subjects affected / exposed	1 / 387 (0.26%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	1	1	0
Vulvovaginal pruritus			

subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood triglycerides increased			
subjects affected / exposed	2 / 387 (0.52%)	1 / 391 (0.26%)	2 / 194 (1.03%)
occurrences (all)	2	1	2
Heart rate increased			
subjects affected / exposed	1 / 387 (0.26%)	2 / 391 (0.51%)	1 / 194 (0.52%)
occurrences (all)	1	2	1
Alanine aminotransferase increased			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	1	0	0
White blood cells urine positive			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Oxygen saturation decreased			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			

subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Procedural pain			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Congenital, familial and genetic disorders			
Patent ductus arteriosus			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	0	0	0
Ankyloglossia congenital			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 387 (2.84%)	11 / 391 (2.81%)	7 / 194 (3.61%)
occurrences (all)	13	14	9
Dizziness			
subjects affected / exposed	1 / 387 (0.26%)	1 / 391 (0.26%)	1 / 194 (0.52%)
occurrences (all)	1	1	1
Disturbance in attention			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Somnolence			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 387 (0.78%)	6 / 391 (1.53%)	2 / 194 (1.03%)
occurrences (all)	3	6	2
Vomiting			
subjects affected / exposed	1 / 387 (0.26%)	2 / 391 (0.51%)	1 / 194 (0.52%)
occurrences (all)	1	2	1

Abdominal pain			
subjects affected / exposed	1 / 387 (0.26%)	1 / 391 (0.26%)	1 / 194 (0.52%)
occurrences (all)	1	1	1
Dyspepsia			
subjects affected / exposed	1 / 387 (0.26%)	1 / 391 (0.26%)	1 / 194 (0.52%)
occurrences (all)	1	1	1
Flatulence			
subjects affected / exposed	1 / 387 (0.26%)	1 / 391 (0.26%)	1 / 194 (0.52%)
occurrences (all)	1	1	1
Abdominal discomfort			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	2	0	2
Constipation			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Gastrointestinal pain			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 387 (0.00%)	2 / 391 (0.51%)	0 / 194 (0.00%)
occurrences (all)	0	2	0
Hepatobiliary disorders			
Cholestasis of pregnancy			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Cholestasis			
subjects affected / exposed	1 / 387 (0.26%)	2 / 391 (0.51%)	1 / 194 (0.52%)
occurrences (all)	1	2	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Urticaria			

subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	1	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 387 (0.00%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	0 / 387 (0.00%)	2 / 391 (0.51%)	0 / 194 (0.00%)
occurrences (all)	0	2	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Neck pain			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Spinal pain			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	3 / 387 (0.78%)	1 / 391 (0.26%)	3 / 194 (1.55%)
occurrences (all)	3	1	3
Cystitis			
subjects affected / exposed	1 / 387 (0.26%)	1 / 391 (0.26%)	1 / 194 (0.52%)
occurrences (all)	1	1	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 387 (0.26%)	1 / 391 (0.26%)	1 / 194 (0.52%)
occurrences (all)	1	1	1

Herpes virus infection			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Rhinitis			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
subjects affected / exposed	2 / 387 (0.52%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	2	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 387 (0.26%)	1 / 391 (0.26%)	1 / 194 (0.52%)
occurrences (all)	1	1	1
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	0 / 194 (0.00%)
occurrences (all)	1	0	0
Escherichia infection			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Bacterial vaginosis			
subjects affected / exposed	1 / 387 (0.26%)	0 / 391 (0.00%)	1 / 194 (0.52%)
occurrences (all)	1	0	1
Urinary tract infection bacterial			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 387 (0.00%)	1 / 391 (0.26%)	0 / 194 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	SET Day 5 - placebo	SET Day 3 - nolasiban	SET Day 3 - placebo
Total subjects affected by non-serious adverse events			

subjects affected / exposed	56 / 196 (28.57%)	36 / 193 (18.65%)	45 / 195 (23.08%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	2
Vasodilatation			
subjects affected / exposed	0 / 196 (0.00%)	1 / 193 (0.52%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Extremity necrosis			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Oocyte harvest			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Cervix cerclage procedure			
subjects affected / exposed	0 / 196 (0.00%)	1 / 193 (0.52%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Abortion induced			
subjects affected / exposed	0 / 196 (0.00%)	1 / 193 (0.52%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Pregnancy, puerperium and perinatal conditions			
Biochemical pregnancy			
subjects affected / exposed	9 / 196 (4.59%)	8 / 193 (4.15%)	12 / 195 (6.15%)
occurrences (all)	9	8	12
Abortion missed			
subjects affected / exposed	6 / 196 (3.06%)	8 / 193 (4.15%)	3 / 195 (1.54%)
occurrences (all)	6	8	3
Abortion spontaneous			
subjects affected / exposed	6 / 196 (3.06%)	5 / 193 (2.59%)	8 / 195 (4.10%)
occurrences (all)	6	5	8
Haemorrhage in pregnancy			

subjects affected / exposed	2 / 196 (1.02%)	1 / 193 (0.52%)	3 / 195 (1.54%)
occurrences (all)	2	2	3
Abortion threatened			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Blighted ovum			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	1	0	0
Abortion incomplete			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	1	0	0
Imminent abortion			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Subchorionic haematoma			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	2	0	0
Vomiting in pregnancy			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Foetal growth restriction			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Placenta praevia			
subjects affected / exposed	1 / 196 (0.51%)	1 / 193 (0.52%)	1 / 195 (0.51%)
occurrences (all)	1	1	1
Polyhydramnios			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Cervical incompetence			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Premature separation of placenta			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	1	0	0
Threatened labour			

subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 196 (0.00%)	1 / 193 (0.52%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 196 (0.00%)	1 / 193 (0.52%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	7 / 196 (3.57%)	2 / 193 (1.04%)	5 / 195 (2.56%)
occurrences (all)	11	2	6
Ovarian hyperstimulation syndrome			
subjects affected / exposed	2 / 196 (1.02%)	1 / 193 (0.52%)	2 / 195 (1.03%)
occurrences (all)	2	2	2
Pelvic pain			
subjects affected / exposed	3 / 196 (1.53%)	2 / 193 (1.04%)	1 / 195 (0.51%)
occurrences (all)	4	3	1
Uterine pain			
subjects affected / exposed	4 / 196 (2.04%)	1 / 193 (0.52%)	0 / 195 (0.00%)
occurrences (all)	4	1	0
Dysmenorrhoea			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Dyspareunia			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Haematosalpinx			

subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Uterine haematoma			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	1	0	0
Uterine haemorrhage			
subjects affected / exposed	0 / 196 (0.00%)	1 / 193 (0.52%)	1 / 195 (0.51%)
occurrences (all)	0	1	1
Vulvovaginal pruritus			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood triglycerides increased			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Heart rate increased			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	1	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 196 (0.00%)	1 / 193 (0.52%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 196 (0.00%)	1 / 193 (0.52%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 196 (0.00%)	1 / 193 (0.52%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
White blood cells urine positive			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Oxygen saturation decreased			

subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 196 (0.00%)	1 / 193 (0.52%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Patent ductus arteriosus			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Ankyloglossia congenital			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 196 (0.00%)	1 / 193 (0.52%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 196 (2.04%)	4 / 193 (2.07%)	7 / 195 (3.59%)
occurrences (all)	5	4	9
Dizziness			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Disturbance in attention			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Somnolence			

subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 196 (2.55%)	1 / 193 (0.52%)	1 / 195 (0.51%)
occurrences (all)	5	1	1
Vomiting			
subjects affected / exposed	2 / 196 (1.02%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	2	0	0
Abdominal pain			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Abdominal discomfort			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal pain			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	1	0	1
Hepatobiliary disorders			
Cholestasis of pregnancy			

subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	1	0	0
Cholestasis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	0 / 196 (0.00%)	1 / 193 (0.52%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Decubitus ulcer			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	2 / 196 (1.02%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	2	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Spinal pain			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0

Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	1	0	0
Herpes virus infection			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Otitis media			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	1	0	0
Vaginal infection			
subjects affected / exposed	0 / 196 (0.00%)	2 / 193 (1.04%)	0 / 195 (0.00%)
occurrences (all)	0	2	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 196 (0.00%)	1 / 193 (0.52%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Escherichia infection			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Bacterial vaginosis			

subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 196 (0.00%)	0 / 193 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 193 (0.00%)	0 / 195 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	All Women Follow-up Set - overall Day 3 and Day 5 - nolasiban	All Women Follow-up Set - overall Day 3 and Day 5 - placebo	All infant set - overall Day 3 and Day 5 - nolasiban
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 137 (33.58%)	43 / 112 (38.39%)	3 / 136 (2.21%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Vasodilatation			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Extremity necrosis			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	1 / 136 (0.74%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Oocyte harvest			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Cervix cerclage procedure			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Abortion induced			

subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Pregnancy, puerperium and perinatal conditions			
Biochemical pregnancy			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Abortion missed			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Abortion spontaneous			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Haemorrhage in pregnancy			
subjects affected / exposed	4 / 137 (2.92%)	3 / 112 (2.68%)	0 / 136 (0.00%)
occurrences (all)	5	3	0
Abortion threatened			
subjects affected / exposed	1 / 137 (0.73%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	1	1	0
Blighted ovum			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Abortion incomplete			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Imminent abortion			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Subchorionic haematoma			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	2	0
Vomiting in pregnancy			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Foetal growth restriction			

subjects affected / exposed	2 / 137 (1.46%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	2	0	0
Placenta praevia			
subjects affected / exposed	5 / 137 (3.65%)	2 / 112 (1.79%)	0 / 136 (0.00%)
occurrences (all)	5	2	0
Polyhydramnios			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Cervical incompetence			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Premature separation of placenta			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Threatened labour			
subjects affected / exposed	1 / 137 (0.73%)	2 / 112 (1.79%)	0 / 136 (0.00%)
occurrences (all)	1	2	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Feeling hot			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	5 / 137 (3.65%)	9 / 112 (8.04%)	0 / 136 (0.00%)
occurrences (all)	5	12	0
Ovarian hyperstimulation syndrome			

subjects affected / exposed	2 / 137 (1.46%)	4 / 112 (3.57%)	0 / 136 (0.00%)
occurrences (all)	4	4	0
Pelvic pain			
subjects affected / exposed	2 / 137 (1.46%)	3 / 112 (2.68%)	0 / 136 (0.00%)
occurrences (all)	2	3	0
Uterine pain			
subjects affected / exposed	1 / 137 (0.73%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	1	1	0
Dysmenorrhoea			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Dyspareunia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Haematosalpinx			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Uterine haematoma			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Uterine haemorrhage			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal pruritus			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood triglycerides increased			
subjects affected / exposed	2 / 137 (1.46%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	2	0	0
Heart rate increased			

subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
White blood cells urine positive			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Oxygen saturation decreased			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Patent ductus arteriosus			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	1 / 136 (0.74%)
occurrences (all)	0	0	1
Ankyloglossia congenital			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	1 / 136 (0.74%)
occurrences (all)	0	0	1

Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 137 (3.65%)	8 / 112 (7.14%)	0 / 136 (0.00%)
occurrences (all)	6	11	0
Dizziness			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 137 (1.46%)	4 / 112 (3.57%)	0 / 136 (0.00%)
occurrences (all)	2	4	0
Vomiting			
subjects affected / exposed	1 / 137 (0.73%)	2 / 112 (1.79%)	0 / 136 (0.00%)
occurrences (all)	1	2	0
Abdominal pain			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	1 / 137 (0.73%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	1	1	0
Flatulence			
subjects affected / exposed	1 / 137 (0.73%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	1	1	0
Abdominal discomfort			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	2	0	0
Constipation			

subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal pain			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 137 (0.00%)	2 / 112 (1.79%)	0 / 136 (0.00%)
occurrences (all)	0	2	0
Hepatobiliary disorders			
Cholestasis of pregnancy			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Cholestasis			
subjects affected / exposed	1 / 137 (0.73%)	2 / 112 (1.79%)	0 / 136 (0.00%)
occurrences (all)	1	2	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	1 / 136 (0.74%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	0 / 137 (0.00%)	2 / 112 (1.79%)	0 / 136 (0.00%)
occurrences (all)	0	2	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue			

disorders			
Groin pain			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 137 (1.46%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	2	1	0
Cystitis			
subjects affected / exposed	1 / 137 (0.73%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 137 (0.73%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	1	1	0
Herpes virus infection			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	0 / 137 (0.00%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			

subjects affected / exposed	1 / 137 (0.73%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	1	1	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Escherichia infection			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Bacterial vaginosis			
subjects affected / exposed	1 / 137 (0.73%)	0 / 112 (0.00%)	0 / 136 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 112 (0.89%)	0 / 136 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	All infant set - overall Day 3 and Day 5 - placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 109 (0.92%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Vasodilatation			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Extremity necrosis			

subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0		
Surgical and medical procedures Oocyte harvest subjects affected / exposed occurrences (all) Cervix cerclage procedure subjects affected / exposed occurrences (all) Abortion induced subjects affected / exposed occurrences (all)	 0 / 109 (0.00%) 0 0 / 109 (0.00%) 0 0 / 109 (0.00%) 0		
Pregnancy, puerperium and perinatal conditions Biochemical pregnancy subjects affected / exposed occurrences (all) Abortion missed subjects affected / exposed occurrences (all) Abortion spontaneous subjects affected / exposed occurrences (all) Haemorrhage in pregnancy subjects affected / exposed occurrences (all) Abortion threatened subjects affected / exposed occurrences (all) Blighted ovum subjects affected / exposed occurrences (all) Abortion incomplete subjects affected / exposed occurrences (all) Imminent abortion	 0 / 109 (0.00%) 0 0 / 109 (0.00%) 0 0 / 109 (0.00%) 0 0 / 109 (0.00%) 0 0 / 109 (0.00%) 0 0 / 109 (0.00%) 0 0 / 109 (0.00%) 0		

subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Subchorionic haematoma			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Vomiting in pregnancy			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Foetal growth restriction			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Placenta praevia			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Polyhydramnios			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Cervical incompetence			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Premature separation of placenta			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Threatened labour			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Feeling hot			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Pain			

subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Ovarian hyperstimulation syndrome			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Pelvic pain			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Uterine pain			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Dysmenorrhoea			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Dyspareunia			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Haematosalpinx			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Uterine haematoma			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Uterine haemorrhage			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Vulvovaginal pruritus			

subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Investigations			
Blood triglycerides increased			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Heart rate increased			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
White blood cells urine positive			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Oxygen saturation decreased			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Post procedural haemorrhage			

subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Congenital, familial and genetic disorders			
Patent ductus arteriosus			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Ankyloglossia congenital			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Disturbance in attention			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		

Abdominal pain subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0		
Dyspepsia subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0		
Flatulence subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0		
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0		
Constipation subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0		
Diarrhoea subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0		
Gastrointestinal pain subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0		
Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0		
Hepatobiliary disorders Cholestasis of pregnancy subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0		
Cholestasis subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0		
Urticaria			

subjects affected / exposed occurrences (all) Decubitus ulcer subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0 0 / 109 (0.00%) 0		
Renal and urinary disorders Cystitis noninfective subjects affected / exposed occurrences (all)	 0 / 109 (0.00%) 0		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	 0 / 109 (0.00%) 0		
Musculoskeletal and connective tissue disorders Groin pain subjects affected / exposed occurrences (all) Musculoskeletal chest pain subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all) Spinal pain subjects affected / exposed occurrences (all)	 0 / 109 (0.00%) 0 0 / 109 (0.00%) 0 0 / 109 (0.00%) 0 0 / 109 (0.00%) 0		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all) Cystitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 0 / 109 (0.00%) 0 0 / 109 (0.00%) 0 0 / 109 (0.00%) 0		

Herpes virus infection			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Otitis media			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Vaginal infection			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Escherichia infection			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Bacterial vaginosis			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Urinary tract infection bacterial			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 109 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Of 778 subjects treated, 249 had confirmed pregnancies at Wk 10. Follow-up (fu) data were provided for 246 fetuses. Pregnancies resulted in live birth for 243 subjects, assuming +ve outcome in case of loss to fu. Neonatal fu data on 245 infants.

Notes: