



## Clinical trial results:

**A randomised, double-blind, parallel groups, placebo-controlled, multi-centre study assessing the effects of a selective oxytocin antagonist (barusiban) and a mixed oxytocin antagonist – vasopressin V1a antagonist (atosiban) administered intravenously on luteal phase uterine contractions in oocyte donors supplemented with vaginal progesterone**

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines

## Summary

EudraCT number	2007-003158-27
Trial protocol	BE PL ES
Global end of trial date	11 September 2008

## Results information

Result version number	v1 (current)
This version publication date	06 January 2017
First version publication date	06 January 2017

## Trial information

### Trial identification

Sponsor protocol code	FE 200440 CS09
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### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00587327
WHO universal trial number (UTN)	-

Notes:

## Sponsors

Sponsor organisation name	Ferring Pharmaceuticals A/S
Sponsor organisation address	Kay Fiskers Plads 11, Copenhagen S, Denmark, 2300
Public contact	Clinical Development Support, Ferring Pharmaceuticals, DK0-Disclosure@fering.com
Scientific contact	Clinical Development Support, Ferring Pharmaceuticals, DK0-Disclosure@fering.com

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	11 September 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 May 2008
Global end of trial reached?	Yes
Global end of trial date	11 September 2008
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the effects of barusiban and atosiban compared to placebo on luteal phase uterine contractions in oocyte donors supplemented with progesterone

Protection of trial subjects:

The trial was performed in accordance with the Declaration of Helsinki and its amendments in force at the initiation of the trial.

Background therapy:

Progesterone (utrogestan), as non-investigational medicinal product (NIMP), was dispensed to subjects who were screened and included in the trial.

Evidence for comparator:

This was a randomised controlled trial with placebo as the comparator to adequately document the efficacy and safety of barusiban and atosiban. A placebo group was justified for this trial as there is no therapy available for this indication.

Actual start date of recruitment	13 November 2007
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	Belgium: 33
Country: Number of subjects enrolled	Czech Republic: 53
Country: Number of subjects enrolled	Spain: 39
Worldwide total number of subjects	125
EEA total number of subjects	125

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)	125
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

A total of 5 sites randomised subjects into the trial : 1 in Belgium, 2 in Spain, and 2 in Czech Republic.

### Pre-assignment

Screening details:

A total of 129 subjects were screened in the trial, of whom 125 subjects were randomised: 41 to barusiban, 42 to atosiban and 42 to placebo.

### Period 1

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

### Arms

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

Arm description:

Subjects randomised to barusiban investigational medicinal product (IMP) were included in this group.

Arm type	Experimental
Investigational medicinal product name	Barusiban
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received barusiban (Intravenous [IV] bolus 9 mg followed by an IV infusion of 2.16 mg/h). The IV bolus volume was 0.9 mL administered over 1 minute and the infusion rate was 24 mL/h for approximately 4 hours. Total amount of exposure to barusiban was 17.64 mg (9.0 mg bolus + 8.64 mg infused).

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

Subjects randomised to atosiban IMP were included in this group.

Arm type	Experimental
Investigational medicinal product name	Atosiban
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received atosiban (IV bolus 6.75 mg followed by an IV infusion of 18 mg/h). The IV bolus volume was 0.9 mL administered over 1 minute and the infusion rate was 24 mL/h for approximately 4 hours. Total amount of exposure to atosiban was 78.75 mg (6.75 mg bolus + 72.0 mg infused).

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

Subjects randomised to placebo IMP were included in this group.

Arm type	Placebo
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received IV bolus of saline (sodium chloride 0.9%) followed by an IV infusion of saline. The IV bolus volume was 0.9 mL administered over 1 minute and the infusion rate was 24 mL/h for approximately 4 hours.

<b>Number of subjects in period 1</b>	Barusiban	Atosiban	Placebo
Started	41	42	42
Completed	41	41	42
Not completed	0	1	0
Adverse event, non-fatal	-	1	-

## Baseline characteristics

### Reporting groups

Reporting group title	Barusiban
Reporting group description:	
Subjects randomised to barusiban investigational medicinal product (IMP) were included in this group.	
Reporting group title	Atosiban
Reporting group description:	
Subjects randomised to atosiban IMP were included in this group.	
Reporting group title	Placebo
Reporting group description:	
Subjects randomised to placebo IMP were included in this group.	

Reporting group values	Barusiban	Atosiban	Placebo
Number of subjects	41	42	42
Age categorical			
Data are presented for the ITT analysis set.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	41	42	42
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	41	42	42
Male	0	0	0

Reporting group values	Total		
Number of subjects	125		
Age categorical			
Data are presented for the ITT analysis set.			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	125		
From 65-84 years	0		
85 years and over	0		

Gender categorical			
Units: Subjects			
Female	125		
Male	0		

### Subject analysis sets

Subject analysis set title	Intention-to-treat (ITT) analysis set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All randomised and exposed subjects providing data on the frequency of uterine contractions 3 hours after start of dosing were included in this analysis set.

Subject analysis set title	Per Protocol (PP) analysis set
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in the ITT analysis set except those who met any of the criteria considered as major protocol deviations were included in this analysis set.

Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomised and exposed subjects were included in this analysis set.

Reporting group values	Intention-to-treat (ITT) analysis set	Per Protocol (PP) analysis set	Safety Analysis Set
Number of subjects	117	112	125
Age categorical			
Data are presented for the ITT analysis set.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	117	112	125
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	117	112	125
Male	0	0	0

## End points

### End points reporting groups

Reporting group title	Barusiban
Reporting group description: Subjects randomised to barusiban investigational medicinal product (IMP) were included in this group.	
Reporting group title	Atosiban
Reporting group description: Subjects randomised to atosiban IMP were included in this group.	
Reporting group title	Placebo
Reporting group description: Subjects randomised to placebo IMP were included in this group.	
Subject analysis set title	Intention-to-treat (ITT) analysis set
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomised and exposed subjects providing data on the frequency of uterine contractions 3 hours after start of dosing were included in this analysis set.	
Subject analysis set title	Per Protocol (PP) analysis set
Subject analysis set type	Per protocol
Subject analysis set description: All subjects in the ITT analysis set except those who met any of the criteria considered as major protocol deviations were included in this analysis set.	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description: All randomised and exposed subjects were included in this analysis set.	

### Primary: Frequency of uterine contractions at 3 hours after start of dosing

End point title	Frequency of uterine contractions at 3 hours after start of dosing
End point description: Data are presented for the ITT analysis set.	
End point type	Primary
End point timeframe: At 3 hours after start of dosing.	

End point values	Barusiban	Atosiban	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	36	36	
Units: contractions/min				
arithmetic mean (standard deviation)	2.72 (± 0.991)	2.81 (± 0.947)	3.14 (± 1.11)	

## Statistical analyses



<b>Statistical analysis title</b>	Frequency at 3 hours- atosiban vs placebo
Statistical analysis description:	
Analysis of contraction frequency at 3 hours after start of dosing was done using analysis of variance (ANOVA) on the ITT analysis set.	
Comparison groups	Placebo v Atosiban
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.166
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.335
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.811
upper limit	0.141

<b>Statistical analysis title</b>	Frequency at 3 hours- barusiban vs placebo
Statistical analysis description:	
Analysis of contraction frequency at 3 hours after start of dosing was done using analysis of variance (ANOVA) on the ITT analysis set.	
Comparison groups	Placebo v Barusiban
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.075
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.426
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.896
upper limit	0.043

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Overall Treatment Period

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs) were presented and evaluated by treatment groups. Data were presented for safety analysis set.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	10.1
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### Reporting groups

Reporting group title	Barusiban
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Reporting group description:

Subjects randomised to barusiban IMP were included in this group.

Reporting group title	Atosiban
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Reporting group description:

Subjects randomised to atosiban IMP were included in this group.

Reporting group title	Placebo
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Reporting group description:

Subjects randomised to placebo IMP were included in this group.

Serious adverse events	Barusiban	Atosiban	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Barusiban	Atosiban	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 41 (7.32%)	1 / 42 (2.38%)	3 / 42 (7.14%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	1 / 42 (2.38%)
occurrences (all)	1	0	1
Syncope vasovagal			

subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	1 / 42 (2.38%) 1	0 / 42 (0.00%) 0
General disorders and administration site conditions Injection site erythema subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1	0 / 42 (0.00%) 0	0 / 42 (0.00%) 0
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1	0 / 42 (0.00%) 0	0 / 42 (0.00%) 0
Reproductive system and breast disorders Ovarian hyperstimulation syndrome subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	0 / 42 (0.00%) 0	1 / 42 (2.38%) 1
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	0 / 42 (0.00%) 0	1 / 42 (2.38%) 1
Infections and infestations Influenza subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1	0 / 42 (0.00%) 0	0 / 42 (0.00%) 0

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 May 2008	Two protocol changes were introduced in this amendment: the inclusion of a new secondary endpoint, and addition of uterine description and transvaginal ultrasound quality parameters.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported