Clinical trial results:
A randomised, double-blind, parallel groups, placebo-controlled, multi-centre trial in oocyte donors assessing the effects of barusiban, a selective oxytocin antagonist, on uterine contractions on the day of embryo transfer

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	2009-012323-29
Trial protocol	CZ ES BE
Global end of trial date	02 December 2010

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 CS11

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01043120
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@ferring.com
Scientific contact	Clinical Development Support, Ferring Pharmaceuticals, DK0-Disclosure@ferring.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	02 December 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 May 2010
Global end of trial reached?	Yes
Global end of trial date	02 December 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effects of barusiban compared to placebo on uterine contractions on the day of embryo transfer.

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:

An ultrasound contrast agent (SONOVUE) was used as non-investigational product (NIMP) during this trial. SONOVUE was administered intrauterinely via an embryo transfer catheter during the mock embryo transfer procedure.

Evidence for comparator:

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

Actual start date of recruitment	02 February 2010
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: 23
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	Czech Republic: 62
Worldwide total number of subjects	99
EEA total number of subjects	99

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)	99
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 4 sites randomised subjects into the trial : 1 in Belgium, 2 in Czech Republic, and 1 in Spain.

Pre-assignment

Screening details:

A total of 102 subjects were screened in the trial, of whom 99 subjects were randomised: 49 to barusiban, and 50 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, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	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 20 mg for 1 minute followed by an IV infusion of 19 mg for up to 59 minutes). The maximum total duration of administration was 60 minutes.

Arm title	Placebo

Arm description:

Subjects randomised to placebo IMP were included in this group.

Arm type	Placebo
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%) for 1 minute followed by an IV infusion of saline for up to 59 minutes.

Number of subjects in period 1	Barusiban	Placebo
Started	49	50
Completed	48	50
Not completed	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	Placebo
Reporting group description:	
Subjects randomised to placebo IMP were included in this group.	

Reporting group values	Barusiban	Placebo	Total
Number of subjects	49	50	99
Age categorical 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)	49	50	99
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	49	50	99
Male	0	0	0

Subject analysis sets	
Subject analysis set title	Intention-to-treat (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomised and exposed subjects 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 the 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)	Per protocol (PP) analysis set	Safety analysis set
Number of subjects	99	78	99

Age categorical 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)	99	78	99
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	99	78	99
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	Placebo
Reporting group description:	
Subjects randomised to placebo IMP were included in this group.	
Subject analysis set title	Intention-to-treat (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomised and exposed subjects 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 the 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: Absolute change from Baseline in frequency of uterine contractions at 30 minutes after start of dosing

End point title	Absolute change from Baseline in frequency of uterine contractions at 30 minutes after start of dosing
End point description:	
Data are presented for the ITT analysis set.	
End point type	Primary
End point timeframe:	
From Baseline to 30 minutes after start of dosing.	

End point values	Barusiban	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	40		
Units: contractions/min				
arithmetic mean (standard deviation)	-0.25 (± 1.52)	0.47 (± 1.26)		

Statistical analyses

Statistical analysis title	Frequency at 30 minutes - barusiban vs placebo
Statistical analysis description:	
Analysis of change in contraction frequency from Baseline at 30 minutes was done using analysis of covariance (ANCOVA) on the ITT analysis set.	
Comparison groups	Barusiban v Placebo

Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.04
upper limit	-0.12

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

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups	
Reporting group title	Barusiban
Reporting group description:	
Subjects randomised to barusiban IMP were included in this group.	
Reporting group title	Placebo
Reporting group description:	
Subjects randomised to placebo IMP were included in this group.	

Serious adverse events	Barusiban	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Barusiban	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 49 (2.04%)	2 / 50 (4.00%)	
Nervous system disorders			
Presyncope			
subjects affected / exposed	1 / 49 (2.04%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 49 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Reproductive system and breast			

disorders Ovarian torsion subjects affected / exposed occurrences (all)	0 / 49 (0.00%) 0	1 / 50 (2.00%) 1	

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

None reported